Entrez PubMed

1: Radiology 1979 Jan;130(1):241-4 Related Articles, NEW **Books**, LinkOut

Pharmacologic enhancement of gallium-67 tumor-to-blood ratios for EMT-6 sarcoma (BALB/c mice).

PubMed Services

Larson SM, Rasey JS, Grunbaum Z, Allen DR.

At various intervals after intravenous injection of carrier-free 67Ga-citrate, iron dextrane or deferoxamine mesylate was injected into EMT-6 tumor-bearing BALB/c mice. After treatment, rapid clearance of 67Ga from soft tissues was observed. Tumor uptake was not greatly affected, and so increased tumor-to-blood ratios were observed. The authors conclude that these drugs can enhance target-to-nontarget uptake ratios for tumors.

Related Resources

PMID: 758657 [PubMed - indexed for MEDLINE]

Display Abstract Sort Save Text Clip Add Order

☐ **1:** U54705. Mus musculus tumo...[gi:1490512]

ProbeSet, Related Sequences, Protein, Taxonomy, UniSTS, LinkOut

```
LOCUS       MMU54705                1432 bp    mRNA    linear   ROD 15-AUG-1996
DEFINITION  Mus musculus tumor supressor maspin mRNA, complete cds.
ACCESSION   U54705
VERSION     U54705.1  GI:1490512
KEYWORDS    .
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 1432)
  AUTHORS   Zhang,M., Nicolai,M. and Sager,R.
  TITLE     Mouse maspin cDNA sequence
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 1432)
  AUTHORS   Zhang,M.
  TITLE     Direct Submission
  JOURNAL   Submitted (11-APR-1996) Ming Zhang, Cancer Genetics, Dana Farber
            Cancer Institute, 44 Binney Street, Boston, MA 02115, USA
COMMENT     On Aug 15, 1996 this sequence version replaced gi:1354502.
FEATURES             Location/Qualifiers
     source          1..1432
                     /organism="Mus musculus"
                     /db_xref="taxon:10090"
     5'UTR           1..189
     CDS             190..1317
                     /function="tumor supressor"
                     /codon_start=1
                     /product="maspin"
                     /protein_id="AAB06042.1"
                     /db_xref="GI:1490513"
                     /translation="MDALRLANSAFAVDLFKQLCERDPAGNILFSPICLSTSLSLAQV
                     GTKGDTANEIGQVLHFENVKDVPFGFQTVTSDVNKLSSFYSLKLVKRLYIDKSLNPST
                     EFISSTKRPYAKELETVDFKDKLEETKGQINSSIKELTDGHFEDILSENSISDQTKIL
                     VVNAAYFVGKWMKKFPESETKECPFRISKTDTKPVQMMNLEATFCLGNIDDISCKIIE
                     LPFQNKHLSMLIVLPKDVEDESTGLEKIEQQLNPETLLQWTNPSTMANAKVKLSLPKF
                     KVEKMIDPKASLESLGLKSLFNESTSDFSGMSETKGVSLSNVIHRVCLEITEDGGESI
                     EVPGSRILQHKDEFNADHPFIYIIRHNKTRNIIFFGKFCSP"
     3'UTR           1318..1432
     polyA site      1432
                     /note="67 A nucleotides"
BASE COUNT      427 a    327 c    293 g    385 t
ORIGIN
        1 ctccttcggc tttttccccc cttttgcatc ttgtttcccg ggatacctgc aactcaaggt
       61 ctaaggtaca aattgcaatc ctgtccatgc acttgtctct aacacaccag tgggtcctat
      121 ctaaggaagc ctttgacctt gagtcgtgaa actgtctctc tgaccttggg gtgcacatcc
      181 tgtccgagga tggatgccct gagactggca aattcagctt ttgctgttga cttgttcaaa
      241 caactatgtg aaagggaccc agcaggaaac attctcttct ctccaatatg cctctctact
      301 tctctgtccc ttgcgcaagt gggcaccaaa ggcgacacag caaatgaaat tggacaggtc
      361 cttcattttg agaatgtcaa agatgtaccc tttgggtttc aaacagtcac ttctgatgtt
```

```
 421 aataagctca gttcttttta ctctttgaaa cttgtcaagc gactctacat agacaaatct
 481 ctgaaccctt ctacagaatt tatcagttct accaaaagac catatgcaaa agaattggaa
 541 actgttgact tcaaagacaa actggaagaa acgaaaggtc aaattaacag ctccattaag
 601 gagctcacag atggccactt tgaggacatt ttgtcagaga acagtataag tgaccagacc
 661 aaaatccttg tggttaatgc tgcctacttt gttggaaagt ggatgaagaa atttccggaa
 721 tcagaaacaa aagaatgtcc tttcagaatc agcaagacag acaccaaacc cgtacaaatg
 781 atgaatcttg aggccacttt ctgcttgggt aacattgatg acatcagctg taagatcata
 841 gaacttcctt tccagaataa gcatctgagt atgctcattg tgctccccaa ggacgtggag
 901 gatgagtcca caggcctgga gaagattgaa cagcaactca acccagaaac attgttacag
 961 tggaccaacc ccagtaccat ggccaatgcc aaagtcaaac tttccctccc aaagtttaag
1021 gtagaaaaga tgattgatcc caaggctagt ctggaaagcc tagggctgaa aagtctcttc
1081 aatgaaagta catcggattt ctctggaatg tcagagacca agggagtgtc cctgtcaaat
1141 gtgattcata gagtatgcct agaaataacc gaagatggtg gtgagtccat cgaggtgcca
1201 gggtcccgga tcttacagca caaggatgaa ttcaatgctg accatccatt tatttatatc
1261 attagacaca acaaaactcg aaacatcatt ttctttggca aattctgttc tccttagctg
1321 gcagggcctt gccaagtctc agggaacttg tctgtagtcg cagagctctg taaactttgt
1381 atccagacaa tcactttcta tacaataaat tgtaaatgtt gctgaatcag ga
//
```

Revised: October 24, 2001.

mel-14 human homolog

☐ **1:** M25280. Human lymph node ...[gi:187182]

Related Sequences, OMIM, Protein, PubMed, Taxonomy, UniSTS, LinkOut

```
LOCUS       HUMLNHR                 2354 bp    mRNA    linear   PRI 07-OCT-1998
DEFINITION  Human lymph node homing receptor mRNA, complete cds.
ACCESSION   M25280
VERSION     M25280.1  GI:187182
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 2354)
  AUTHORS   Siegelman,M.H. and Weissman,I.L.
  TITLE     Human homologue of mouse lymph node homing receptor: evolutionary
            conservation at tandem cell interaction domains
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 86 (14), 5562-5566 (1989)
  MEDLINE   89315837
COMMENT     Draft entry and computer-readable sequence for [1] kindly provided
            by M.H.Siegelman, 02-JUN-1989.
FEATURES             Location/Qualifiers
     source          1..2354
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
     gene            1..2354
                     /gene="LNHR"
     CDS             116..1234
                     /gene="LNHR"
                     /note="lymph node homing receptor precursor"
                     /codon_start=1
                     /protein_id="AAC63053.1"
                     /db_xref="GI:307134"
                     /db_xref="GDB:G00-118-834"
                     /translation="MIFPWKCQSTQRDLWNIFKLWGWTMLCCDFLAHHGTDCWTYHYS
                     EKPMNWQRARRFCRDNYTDLVAIQNKAEIEYLEKTLPFSRSYYWIGIRKIGGIWTWVG
                     TNKSLTEEAENWGDGEPNNKKNKEDCVEIYIKRNKDAGKWNDDACHKLKAALCYTASC
                     QPWSCSGHGECVEIINNYTCNCDVGYYGPQCQLVIQCEPLEAPELGTMDCTHPLGNFS
                     FSSQCAFSCSEGTNLTGIEETTCGPFGNWSSPEPTCQVIQCEPLSAPDLGIMNCSHPL
                     ASFSFTSACTFICSEGTELIGKKKTICESSGIWSNPSPICQKLDKSFSMIKEGDYNPL
                     FIPVAVMVTAFSGLAFIIWLARRLKKGKKSKRSMNDPY"
     sig peptide     116..229
                     /gene="LNHR"
                     /note="lymph node homing receptor signal peptide"
BASE COUNT      663 a    531 c    498 g    662 t
ORIGIN
        1 gagtgcagtc tacctgcagc acagcacact cctttgggca aggacctgag acccttgtgc
       61 taagtcaaga ggctcaatgg gctgcagaag aactagagaa ggaccaagca aagccatgat
      121 atttccatgg aaatgtcaga gcacccagag ggacttatgg aacatcttca agttgtgggg
      181 gtggacaatg ctctgttgtg atttcctggc acatcatgga accgactgct ggacttacca
      241 ttattctgaa aaacccatga actggcaaag ggctagaaga ttctgccgag acaattacac
      301 agatttagtt gccatacaaa acaaggcgga aattgagtat ctggagaaga ctctgccttt
      361 cagtcgttct tactactgga taggaatccg gaagatagga ggaatatgga cgtgggtggg
```

no hits

```
 421 aaccaacaaa tctcttactg aagaagcaga gaactgggga gatggtgagc ccaacaacaa
 481 gaagaacaag gaggactgcg tggagatcta tatcaagaga aacaaagatg caggcaaatg
 541 gaacgatgac gcctgccaca aactaaaggc agccctctgt tacacagctt cttgccagcc
 601 ctggtcatgc agtggccatg gagaatgtgt agaaatcatc aataattaca cctgcaactg
 661 tgatgtgggg tactatgggc cccagtgtca gcttgtgatt cagtgtgagc ctttggaggc
 721 cccagagctg ggtaccatgg actgtactca ccctttggga aacttcagct tcagctcaca
 781 gtgtgccttc agctgctctg aaggaacaaa cttaactggg attgaagaaa ccacctgtgg
 841 accatttgga aactggtcat ctccagaacc aacctgtcaa gtgattcagt gtgagcctct
 901 atcagcacca gatttgggga tcatgaactg tagccatccc ctggccagct tcagctttac
 961 ctctgcatgt accttcatct gctcagaagg aactgagtta attgggaaga agaaaaccat
1021 ttgtgaatca tctggaatct ggtcaaatcc tagtccaata tgtcaaaaat tggacaaaag
1081 tttctcaatg attaaggagg gtgattataa ccccctcttc attccagtgg cagtcatggt
1141 tactgcattc tctgggttgg catttatcat ttggctggca aggagattaa aaaaaggcaa
1201 gaaatccaag agaagtatga atgacccata ttaaatcgcc cttggtgaaa gaaaattctt
1261 ggaatactaa aaatcatgag atcctttaaa tccttccatg aaacgttttg tgtggtggca
1321 cctcctacgt caaacatgaa gtgtgtttcc ttcagtgcat ctgggaagat ttctacccga
1381 ccaacagttc cttcagcttc catttcgccc ctcatttatc cctcaacccc cagcccacag
1441 gtgtttatac agctcagctt tttgtctttt ctgaggagaa acaaataaga ccataaaggg
1501 aaaggattca tgtggaatat aaagatggct gactttgctc tttcttgact cttgttttca
1561 gtttcaattc agtgctgtac ttgatgacag acacttctaa atgaagtgca aatttgatac
1621 atatgtgaat atggactcag ttttcttgca gatcaaattt cacgtcgtct tctgtatact
1681 gtggaggtac actcctatag aaagttcaaa aagtctacgc tctcctttct ttctaactcc
1741 agtgaagtaa tggggtcctg ctcaagttga aagagtccta tttgcactgt agcctcgccg
1801 tctgtgaatt ggaccatcct atttaactgg cttcagcctc cccaccttct tcagccacct
1861 ctctttttca gttggctgac ttccacacct agcatctcat gagtgccaag caaaaggaga
1921 gaagagagaa atagcctgcg ctgtttttta gtttgggggt tttgctgttt ccttttatga
1981 gacccattcc tatttcttat agtcaatgtt tcttttatca cgatattatt agtaagaaaa
2041 catcactgaa atgctagctg caagtgacat ctctttgatg tcatatggaa gagttaaaac
2101 aggtggagaa attccttgat tcacaatgaa atgctctcct ttcccctgcc cccagaactt
2161 ttatccactt acctagattc tacatattct ttaaatttca tctcaggcct ccctcaaccc
2221 caccacttct tttataacta gtcctttact aatccaaccc atgatgagct cctcttcctg
2281 gcttcttact gaaaggttac cctgtaacat gcaattttgc atttgaataa agcctgcttt
2341 ttaagtggga attc
```

//

Revised: October 24, 2001.

1: U04313. Human maspin mRNA...[gi:453368]

Related Sequences, OMIM, Protein, PubMed, Taxonomy, UniSTS, LinkOut

```
LOCUS       HSU04313                2566 bp    mRNA    linear   PRI 11-JUN-1994
DEFINITION  Human maspin mRNA, complete cds.
ACCESSION   U04313
VERSION     U04313.1  GI:453368
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 2566)
  AUTHORS   Zou,Z., Anisowicz,A., Hendrix,M.J., Thor,A., Neveu,M., Sheng,S.,
            Rafidi,K., Seftor,E. and Sager,R.
  TITLE     Maspin, a serpin with tumor-suppressing activity in human mammary
            epithelial cells
  JOURNAL   Science 263 (5146), 526-529 (1994)
  MEDLINE   94120413
   PUBMED   8290962
REFERENCE   2  (bases 1 to 2566)
  AUTHORS   Anisowicz,A.
  TITLE     Direct Submission
  JOURNAL   Submitted (10-DEC-1993) Anthony Anisowicz, Cancer Genetics, Dana
            Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, USA
FEATURES             Location/Qualifiers
     source          1..2566
                     /organism="Homo sapiens"
                     /isolate="76N"
                     /db_xref="taxon:9606"
                     /clone="Z32-1"
                     /sex="female"
                     /cell_line="76N"
                     /cell_type="epithelial"
                     /tissue_type="mammary"
                     /clone_lib="76N cDNA library in lambda Zap II"
     5'UTR           1..75
     CDS             76..1203
                     /codon_start=1
                     /product="maspin"
                     /protein_id="AAA18957.1"
                     /db_xref="GI:453369"
                     /translation="MDALQLANSAFAVDLFKQLCEKEPLGNVLFSPICLSTSLSLAQV
                     GAKGDTANEIGQVLHFENVKDIPFGFQTVTSDVNKLSSFYSLKLIKRLYVDKSLNLST
                     EFISSTKRPYAKELETVDFKDKLEETKGQINNSIKDLTDGHFENILADNSVNDQTKIL
                     VVNAAYFVGKWMKKFPESETKECPFRLNKTDTKPVQMMNMEATFCMGNIDSINCKIIE
                     LPFQNKHLSMFILLPKDVEDESTGLEKIEKQLNSESLSQWTNPSTMANAKVKLSIPKF
                     KVEKMIDPKACLENLGLKHIFSEDTSDFSGMSETKGVALSNVIHKVCLEITEDGGDSI
                     EVPGARILQHKDELNADHPFIYIIRHNKTRNIIFFGKFCSP"
     misc_feature    1093..1098
                     /note="putative serpin reactive center"
     3'UTR           1201..2566
```

```
     polyA signal    2545..2550
BASE COUNT      786 a    526 c    504 g    750 t
ORIGIN
        1 ggcacgagtt gtgctcctcg cttgcctgtt ccttttccac gcattttcca ggataactgt
       61 gactccaggc ccgcaatgga tgccctgcaa ctagcaaatt cggcttttgc cgttgatctg
      121 ttcaaacaac tatgtgaaaa ggagccactg ggcaatgtcc tcttctctcc aatctgtctc
      181 tccacctctc tgtcacttgc tcaagtgggt gctaaaggtg acactgcaaa tgaaattgga
      241 caggttcttc attttgaaaa tgtcaaagat atacccttttg gatttcaaac agtaacatcg
      301 gatgtaaaca aacttagttc cttttactca ctgaaactaa tcaagcggct ctacgtagac
      361 aaatctctga atctttctac agagttcatc agctctacga agagacccta tgcaaaggaa
      421 ttggaaactg ttgacttcaa agataaattg gaagaaacga aaggtcagat caacaactca
      481 attaaggatc tcacagatgg ccactttgag aacattttag ctgacaacag tgtgaacgac
      541 cagaccaaaa tccttgtggt taatgctgcc tactttgttg gcaagtggat gaagaaattt
      601 cctgaatcag aaacaaaaga atgtcctttc agactcaaca agacagacac caaaccagtg
      661 cagatgatga acatggaggc cacgttctgt atgggaaaca ttgacagtat caattgtaag
      721 atcatagagc ttccttttca aaataagcat ctcagcatgt tcatcctact acccaaggat
      781 gtggaggatg agtccacagg cttggagaag attgaaaaac aactcaactc agagtcactg
      841 tcacagtgga ctaatcccag caccatggcc aatgccaagg tcaaactctc cattccaaaa
      901 tttaaggtgg aaaagatgat tgatcccaag gcttgtctgg aaaatctagg gctgaaacat
      961 atcttcagtg aagacacatc tgatttctct ggaatgtcag agaccaaggg agtggcccta
     1021 tcaaatgtta tccacaaagt gtgcttagaa ataactgaag atggtgggga ttccatagag
     1081 gtgccaggag cacggatcct gcagcacaag gatgaattga atgctgacca tccctttatt
     1141 tacatcatca ggcacaacaa aactcgaaac atcattttct ttggcaaatt ctgttctcct
     1201 taagtggcat agcccatgtt aagtcctccc tgacttttct gtggatgccg atttctgtaa
     1261 actctgcatc cagagattca ttttctagat acaataaatt gctaatgttg ctggatcagg
     1321 aagccgccag tacttgtcat atgtagcctt cacacagata gacctttttt tttttccaat
     1381 tctatctttt gtttcctttt ttcccataag acaatgacat acgcttttaa tgaaaaggaa
     1441 tcacgttaga ggaaaaatat ttattcatta tttgtcaaat tgtccggggt agttggcaga
     1501 aatacagtct tccacaaaga aaattcctat aaggaagatt tggaagctct tcttcccagc
     1561 actatgcttt ccttctttgg gatagagaat gttccagaca ttctcgcttc cctgaaagac
     1621 tgaagaaagt gtagtgcatg ggacccacga aactgccctg gctccagtga aacttgggca
     1681 catgctcagg ctactatagg tccagaagtc cttatgttaa gccctggcag gcaggtgttt
     1741 attaaaattc tgaattttgg ggattttcaa aagataatat tttacataca ctgtatgtta
     1801 tagaacttca tggatcagat ctggggcagc aacctataaa tcaacacctt aatatgctgc
     1861 aacaaaatgt agaatattca gacaaaatgg atacataaag actaagtagc ccataagggg
     1921 tcaaaatttg ctgccaaatg cgtatgccac caacttacaa aaacacttcg ttcgcagagc
     1981 ttttcagatt gtggaatgtt ggataaggaa ttatagacct ctagtagctg aaatgcaaga
     2041 ccccaagagg aagttcagat cttaatataa attcactttc atttttgata gctgtcccat
     2101 ctggtcatgt ggttggcact agactggtgg caggggcttc tagctgactc gcacagggat
     2161 tctcacaata gccgatatca gaatttgtgt tgaaggaact tgtctcttca tctaatatga
     2221 tagcgggaaa aggagaggaa actactgcct ttagaaaata taagtaaagt gattaaagtg
     2281 ctcacgttac cttgacacat agtttttcag tctatgggtt tagttacttt agatggcaag
     2341 catgtaactt atattaatag taatttgtaa agttgggtgg ataagctatc cctgttgccg
     2401 gttcatggat tacttctcta taaaaaatat atatttacca aaaaattttg tgacattcct
     2461 tctcccatct cttccttgac atgcattgta aataggttct tcttgttctg agattcaata
     2521 ttgaatttct cctatgctat tgacaataaa atattattga actacc
//
```

Revised: October 24, 2001.

☐ **1:** L24118. Mouse primary res...[gi:400371]

ProbeSet, Related Sequences, Protein, PubMed, Taxonomy, UniSTS, LinkOut

```
LOCUS       MUSB94A                 3512 bp    mRNA    linear   ROD 14-JUL-1994
DEFINITION  Mouse primary response gene B94 mRNA, 3'end.
ACCESSION   L24118
VERSION     L24118.1  GI:400371
KEYWORDS    .
SOURCE      Mus musculus cDNA to mRNA.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 3512)
  AUTHORS   Wolf,F.W., Sarma,V., Seldin,M., Drake,S., Suchard,S.J., Shao,H.,
            O'Shea,K.S. and Dixit,V.M.
  TITLE     B94, a primary response gene inducible by tumor necrosis
            factor-alpha, is expressed in developing hematopoietic tissues and
            the sperm acrosome
  JOURNAL   J. Biol. Chem. 269 (5), 3633-3640 (1994)
  MEDLINE   94148868
   PUBMED   8106408
FEATURES             Location/Qualifiers
     source          1..3512
                     /organism="Mus musculus"
                     /db_xref="taxon:10090"
     CDS             106..2058
                     /codon_start=1
                     /protein_id="AAA72044.1"
                     /db_xref="GI:402160"
                     /translation="MSEASSEDLMPSPEAPDGEEESAKKKEKKSKGLANMFSVFTKGK
                     KKKKDQPRLSDLEVQPKPRPELDGPLPTVEELKEALEHGRLEVAWQVLALERQLEAAA
                     AAGGMSNEELVWRQSKVEALYVLLCDQVLGVLRRPLEAAPERLSQALAVVSQEELEDR
                     RASGGPLAAALEATRPRRWLQRWRGVVAEVAAERLDAQPATAPEGRSEAESRFLHMGR
                     TMKEDLEVVVERLKPLFPDEFNVVRTYAESYHYHFASHLCALAQFELCERDTYLLLLW
                     VQNLYPNDILNSPKLAQELQGVGLGSLLPPKQIRLLEAMFLSNEVTSVKQLMARALEL
                     ESQRWTQDVAPQSLDGHCHSELAIDILQIISQGQTKAENITSDVGMQIKQLLLVELAA
                     LLRSYQRAFDEFLEKSKLLRNYRVNIMANINNCLFFWTSVEQKWQISHDSLNRLLEPL
                     KDLKAHGFDTLLQSLFLDLKPLFKKFTQTRWANPVETLEEIITTVSSSLPEFSELQDC
                     FREELMETVHLHLVKEYIIRLCKRRLVLKTAEQQQQLARHILANADAIQGFCTENGST
                     ATWLHRALPMIAEIIRLQDSSAIKIEVATYATWYPDFSKGHLNAILAIKGNLPSSEVR
                     SIRNILDINTGVQEPPRPLFSLIKVT"
BASE COUNT      792 a    965 c    993 g    762 t
ORIGIN
        1 ttcttccaag ggtttcctgg ccagcagtct gtgccaggga ccctgaactt cgctgtaagc
       61 ccccaaaagc cacgctctac atccgaggct gaatcagaga cctccatgtc tgaggcgtcc
      121 tctgaggacc tgatgccatc cccggaggct cccgatgggg aggaggagtc tgcgaagaag
      181 aaggagaaga agtccaaagg actggccaac atgttcagtg tcttcaccaa agggaaaaag
      241 aaaaaaaagg accagcccag attatcagat ctggaagtgc agcccaagcc caggcccgag
      301 ttagatggtc cactgcccac agtggaggag ctcaaggagg ccctggagca cgggcggctg
      361 gaggtggcct ggcaggtgct ggcgttggag aggcagctcg aggctgcggc agcggcgggt
      421 ggcatgagca acgaggagct ggtgtggcgg cagagcaagg tggaggctct gtacgtgctg
      481 ctttgcgacc aggtgctcgg ggtactgcgg cggccgctgg aggcggcgcc cgagcggctg
```

```
 541 agccaggcgc tagccgtggt gtcgcaggag gagctcgagg accggcgggc gtccggggga
 601 cccttggcgg cggcactgga ggccacgcgc ccgcggcgat ggctgcagcg gtggaggggc
 661 gtcgtggcgg aggtggcagc ggaacgtctg gacgcgcagc cggccacagc gcccgagggc
 721 cgctcggagg cggagagcag gttcctgcac atgggtcgca ccatgaagga ggacctggag
 781 gtggtggtgg agaggctgaa gccgctgttc cccgacgagt tcaacgtcgt gcgcacctac
 841 gccgaaagct accactacca cttcgccagc cacctgtgcg ccttggcgca gttcgagttg
 901 tgtgaaaggg atacctactt gctgctgctc tgggtgcaga acctctaccc caatgatatt
 961 ctcaacagcc cgaagttggc acaggagctt caaggtgtcg ggcttgggag cctcctgccc
1021 ccaaagcaga tcagattgct ggaggccatg ttcttgtcca atgaggtgac cagcgtgaag
1081 cagctcatgg cccgagcttt agagctggag tctcagcgct ggacccagga tgtggctccc
1141 cagagcctgg atggccactg tcacagtgag ctggccatcg acattctcca gatcatttca
1201 caaggccaga ctaaggctga gaacatcact tcggacgtgg ggatgcagat aaagcagttg
1261 ctgctggtgg agctggctgc actactgagg agctaccagc gcgcctttga tgagtttcta
1321 gagaagagca aactcctgag gaattacaga gtcaacatca tggccaacat caacaactgc
1381 ctgttcttct ggacttccgt ggagcagaaa tggcagatat ctcatgattc tctgaaccgc
1441 ctgctggagc ctttgaaaga cctcaaggcc catggcttcg acaccctgct ccagagccta
1501 tttttggacc tgaagccgct gtttaagaag ttcacacaga cccgttgggc aaatccagtt
1561 gagaccctgg aggaaatcat cactactgtg agcagcagcc tgcctgaatt ctcagagctg
1621 caggactgtt tccgggagga gctcatggag actgtgcacc tgcacctagt gaaagaatac
1681 atcatcaggc tctgcaaacg gcgcctggtc ctcaagacgg ccgagcagca gcagcagctg
1741 gcaaggcaca tcctggccaa cgcggatgcc attcaggggt tctgcactga gaatggctcc
1801 actgcaacct ggctgcaccg cgccctccct atgattgctg agatcattcg cctgcaagat
1861 tccagtgcca ttaagatcga ggtggccaca tacgccactt ggtaccctga cttcagcaaa
1921 ggccacctga acgccatcct ggccatcaag ggcaatctac caagcagtga agtcaggagc
1981 atccggaaca tactggacat caacacggga gtgcaggagc ctcccaggcc cctgttctcc
2041 cttataaagg ttacttagct tttctgaagg tctgatatgc taatgaggcc cagggaacac
2101 caggcaccac accagttggg gatgctcagt ggctccagct ccatgaccca tcatcaggct
2161 cccacattct gctgttgctt ctgcccagcc ctggctctgg aacaagatct gacagccaag
2221 atcgcacaga tgatggatcc agtggggtcc agacctcact gaagggagct gacatctgag
2281 catgcaagag atttcttgta aatgattatt catcttgggt agagtgacct ttgtctacct
2341 acactgtagt ctgcctttta acggtctgag ttgccctgtc cagctcccta ggatcagggg
2401 tgaagcctca tttataccat ttccttcagc ccagggatgt catgagatag aactaaaaac
2461 aagggaagaa agaagaacta gtatctgacc cggggcctgg aagcaggcct gtgaagtgcc
2521 catgacagag ctagaccctg caaagtgtcc cctggtacca ctcagctagc aggaccctct
2581 tattcactcc ccatgggctg ccctgccccc ctgtgtgtgt atggatgtgt ttgggaagtg
2641 accctggaag ccttcgcaga gcagggacct cccgggttct ctcagatcaa atcttcttgc
2701 atttaggaat aagccagagg ccaccgtctg gagtctggtg ggagtgcagg ggtctggcaa
2761 gtgctttact ggcttcctgt tggtgctgtg ccaaacttcc acggcaagtg ggcttgaact
2821 accacttttc cttcagttct gcaaatcaca agtctattat cagactgaag tctaaatgtg
2881 gtcagggccc actgcctctg gaagccccag ggagaattgt ttcctggtct tccccagtct
2941 ttagaggtta cccccatctt ttgtctgagg accttgtacc ttcagagcca gggacagcta
3001 catatgctcc tcacaccacc acagtctcca ctggttcgga tcccactgtg acttaggatc
3061 cccgtgactg cagtgaatct gcccagagac tcagcagcca ccccattaac taactcctgt
3121 cacccaatag tcattggctc tggggaccag tgggtcccac gggggctaca ctggaaaaca
3181 gcaaggcagt ttgccatcaa ggcacctgct actccacaga tcctgctcct ctctagccat
3241 gagagctctt ctcggcactg gcccagcctt gacttgtcat gattcgaggc tgggatttga
3301 agcttctcct ctgtcccctc ccccaggtac ttgctggagc tggccagggt gagcagcaca
3361 cacagccttt gtattcttgt agacgaccgc tgttgatgac attaatattg ttaatattat
3421 ttttatagtg ttggttttgt atgtgtgtac tcaggacaga atccagagat ttctttttta
3481 tatagcttga tataaaacag atttcaaaag tg
//
```

Revised: October 24, 2001.

1: M25324. Mouse peripheral ...[gi:198803]

ProbeSet, Related Sequences, OMIM, Protein, PubMed, Taxonomy, UniSTS, LinkOut

```
LOCUS       MUSLHR                  2199 bp    mRNA    linear   ROD 27-APR-1993
DEFINITION  Mouse peripheral lymph node-specific homing receptor (MEL-14
            antigen) mRNA, complete cds.
ACCESSION   M25324
VERSION     M25324.1  GI:198803
KEYWORDS    lymphocyte homing receptor.
SOURCE      Mouse (strain ICR) 16 week old female spleen, cDNA to mRNA.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 2199)
  AUTHORS   Lasky,L.A., Singer,M.S., Yednock,T.A., Dowbenko,D., Fennie,C.,
            Rodriguez,H., Nguyen,T., Stachel,S. and Rosen,S.D.
  TITLE     Cloning of a lymphocyte homing receptor reveals a lectin domain
  JOURNAL   Cell 56 (6), 1045-1055 (1989)
  MEDLINE   89168433
   PUBMED   2647302
FEATURES             Location/Qualifiers
     source          1..2199
                     /organism="Mus musculus"
                     /strain="ICR"
                     /db_xref="taxon:10090"
                     /sex="female"
                     /tissue_type="spleen"
                     /dev_stage="16-week old"
     gene            1..2199
                     /gene="Lecam1"
     CDS             106..1224
                     /gene="Lecam1"
                     /codon_start=1
                     /product="lymphocyte homing receptor"
                     /protein_id="AAA39431.1"
                     /db_xref="GI:198804"
                     /translation="MVFPWRCEGTYWGSRNILKLWVWTLLCCDFLIHHGTHCWTYHYS
                     EKPMNWENARKFCKQNYTDLVAIQNKREIEYLENTLPKSPYYYWIGIRKIGKMWTWVG
                     TNKTLTKEAENWGAGEPNNKKSKEDCVEIYIKRERDSGKWNDDACHKRKAALCYTASC
                     QPGSCNGRGECVETINNHTCICDAGYYGPQCQYVVQCEPLEAPELGTMDCIHPLGNFS
                     FQSKCAFNCSEGRELLGTAETQCGASGNWSSPEPICQVVQCEPLEAPELGTMDCIHPL
                     GNFSFQSKCAFNCSEGRELLGTAETQCGASGNWSSPEPICQETNRSFSKIKEGDYNPL
                     FIPVAVMVTAFSGLAFLIWLARRLKKGKKSQERMDDPY"
     sig_peptide     106..219
                     /gene="Lecam1"
     mat_peptide     220..1221
                     /gene="Lecam1"
                     /product="lymphocyte homing receptor"
     polyA_site      2199
                     /gene="Lecam1"
BASE COUNT      626 a    519 c    483 g    571 t
ORIGIN
```

```
     1 gaattctcga gctcgtcgac cacgccctcc ttgtgcaaga actctgagcc ccaggtgcag
    61 gaggctgagg cctgcagaga gacttgcaga gagacccagc aagccatggt gtttccatgg
   121 agatgtgagg gtacttactg gggctcgagg aacatcctga agctgtgggt ctggacactg
   181 ctctgttgtg acttcctgat acaccatgga actcactgtt ggacttacca ttattctgaa
   241 aagcccatga actgggaaaa tgctagaaag ttctgcaagc aaaattacac agatttagtc
   301 gccatacaaa acaagagaga aattgagtat ttagagaata cattgcccaa aagcccttat
   361 tactactgga taggaatcag gaaaattggg aaaatgtgga catgggtggg aaccaacaaa
   421 actctcacta aagaagcaga gaactggggt gctggggagc ccaacaacaa gaagtccaag
   481 gaggactgtg tggagatcta tatcaagagg gaacgagact ctgggaaatg gaacgatgac
   541 gcctgtcaca aacgaaaggc agctctctgc tacacagcct cttgccagcc agggtcttgc
   601 aatggccgtg gagaatgtgt ggaaactatc aacaatcaca cgtgcatctg tgatgcaggg
   661 tattacgggc cccagtgtca gtatgtggtc cagtgtgagc ctttggaggc ccctgagttg
   721 ggtaccatgg actgcatcca ccccttggga aacttcagct tccagtccaa gtgtgctttc
   781 aactgttctg agggaagaga gctacttggg actgcagaaa cacagtgtgg agcatctgga
   841 aactggtcat ctccagagcc aatctgccaa gtggtccagt gtgagccttt ggaggccccc
   901 gagttgggta ccatggactg catccacccc ttgggaaact tcagcttcca gtccaagtgt
   961 gctttcaact gttctgaggg aagagagcta cttgggactg cagaaacaca gtgtggagca
  1021 tctggaaact ggtcatctcc agagccaatc tgccaagaga caaacagaag tttctcaaag
  1081 atcaaagaag gtgactacaa ccccctcttc attcctgtag ccgtcatggt caccgcattc
  1141 tcggggctgg catttctcat ttggctggca aggcggttaa aaaaaggcaa gaaatctcaa
  1201 gaaaggatgg atgatccata ctgattcatc ctttgtgaaa ggaaagccat gaagtgctaa
  1261 agacaaaaca ttggaaaata acgtcaagtc ctcccgtgaa gattttacac gcaggcatct
  1321 cccacattag agatgcagtg tttgctcaac gaatctggaa ggatttcttc atgaccaaca
  1381 gctcctccta atttcccctc gctcattcat cccattaacc ctatcccata atgtgtgtct
  1441 atacagagta gtattttatc atcttttctg tggaggaaca agcaaaagtg ttactgtaga
  1501 atataaagac agctgctttt actctttcct aactcttgtt tcctagttca attcagcaca
  1561 gaagctaatg ccaaacacag tgaaaatatg atccatgagt aattggaaac tcagactcct
  1621 tgcgcatagt acgtacccta tgtaacatcg acaaaaatct ttcatttcca cctccaaaga
  1681 acagtgctct attcaagttg ggaaagtcct acttcctctg tagacccact atctgtgagt
  1741 gacagccact gtagctgttc acattaacct tccccatctc cttttcctag gagaataatt
  1801 ccacacactg caccccatga tggccaccaa acatcaaaga agggaaaatc tcctgcattg
  1861 agttttagtt ttgagttttc ccttctcttt attagatctc tgatggttcc ttgaagtcag
  1921 tgttctgatg attattaata gttaatgata acacaaccca ctctcttgga gctgatgtta
  1981 tgaagacaac aggtagaaaa attcctgggc tcaggctgga gtgacaccct tttctttccc
  2041 taacatcttc tactcagata cctaaattta agattcagga cagctgtccc caactcttac
  2101 catgtctttt ataacttgct ccttaacttg cccaacctgt aggctatctc attttctcgc
  2161 ttcactctgc aaggtttata acatgatgaa tttaaatac
//
```

Revised: October 24, 2001.

1: X85993. M.musculus mRNA f...[gi:854329]

ProbeSet, Related Sequences, Protein, PubMed, Taxonomy, LinkOut

```
LOCUS       MMRNASEMD               2913 bp    mRNA    linear   ROD 08-JUL-1996
DEFINITION  M.musculus mRNA for semaphorin D.
ACCESSION   X85993
VERSION     X85993.1  GI:854329
KEYWORDS    semaphorin; semD gene.
SOURCE      house mouse.
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (bases 1 to 2913)
  AUTHORS   Puschel,A.W., Adams,R.H. and Betz,H.
  TITLE     Murine semaphorin D/collapsin is a member of a diverse gene family
            and creates domains inhibitory for axonal extension
  JOURNAL   Neuron 14 (5), 941-948 (1995)
  MEDLINE   95267431
REFERENCE   2  (bases 1 to 2913)
  AUTHORS   Adams,R.H.
  TITLE     Direct Submission
  JOURNAL   Submitted (30-MAR-1995) R.H. Adams, Max-Planck-Institute fuer
            Hirnforschung, Deutschordenstr. 46, D- 60528 Frankfurt, FRG
COMMENT     Sequence overlapping with those under the acc#U02528, L26080,
            L26081 & L26082.
FEATURES             Location/Qualifiers
     source          1..2913
                     /organism="Mus musculus"
                     /strain="NMRI"
                     /db_xref="taxon:10090"
                     /clone="semaf18"
                     /clone="semae9"
                     /clone_lib="Stratagene lambda ZAP"
                     /dev_stage="12 days embryo"
     gene            111..2429
                     /gene="semD"
     CDS             111..2429
                     /gene="semD"
                     /codon_start=1
                     /product="semaphorin D"
                     /protein_id="CAA59985.1"
                     /db_xref="GI:854330"
                     /db_xref="MGD:107558"
                     /db_xref="SPTREMBL:Q62180"
                     /translation="MGWFTGIACLFWGVLLTARANYANGKNNVPRLKLSYKEMLESNN
                     VITFNGLANSSSYHTFLLDEERSRLYVGAKDHIFSFNLVNIKDFQKIVWPVSYTRRDE
                     CKWAGKDILKECANFIKVLEAYNQTHLYACGTGAFHPICTYIEVGHHPEDNIFKLQDS
                     HFENGRGKSPYDPKLLTASLLIDGELYSGTAADFMGRDFAIFRTLGDHHPIRTEQHDS
                     RWLNDPRFISAHLIPESDNPEDDKVYFFFRENAIGGEHSGKATHARIGQICKNDFGGH
                     RSLVNKWTTFLKARLICSVPGPNGIDTHFDELQDVFLMNSKDPKNPIVYGVFTTSSNI
                     FKGSAVCMYSMSDVRRVFLGPYAHRDGPNYQWVPYQGRVPYPRPGTCPSKTFGGFDST
                     KDLPDDVITFGRSHPAMYNPVFPINNRPIMIKTDVNYQFTQIVVDRVDAEDGQYDVMF
```

```
                     IGTDVGTVLKVVSVPKETWHDLEEVLLEEMTVFREPTTISAMELSTKQQQLYIGSTAG
                     VAQLPLHRCDIYGKACAECCLARDPYCAWDGSSCSRYFPTAKRRTRRQDIRNGDPLTH
                     CSDLEDHDNHHGPSLEERIIYGVENSSTFLECSPKSQRALVYWQFQRRNRRSKREIRM
                     GDHIIRTEQGLLLRSLQKKDSGNYLCHAVEHGFMQTLLKVTLEVIDTEHLEELLHKDD
                     DGDGSKIKEMSSSMTPSQKVWYRDFMQLINHPNLNTMDEFCEQVWKRDRKQRRQRPGH
                     SQGSSNKWKHMQESKKGRNRRTHEFERAPRSV"
BASE COUNT      888 a    632 c    679 g    714 t
ORIGIN
        1 actgatctaa atcacctgtt acctccagtt tccagattgt ttgaacttct ctggacgcac
       61 aatacaggaa ggaaggctgt cgcagctcag ggacctccag cgtctgcagc atgggctggt
      121 tcactgggat tgcctgtctt ttctggggtg tattacttac agccagagca aactatgcaa
      181 acggaaagaa caatgtgcca agactgaaat tatcgtacaa agaaatgttg gaatccaaca
      241 atgtgatcac ttttaatggc ttggccaaca gctccagtta ccacaccttc cttctggatg
      301 aagaacggag tagactatat gttggagcaa aagatcatat attttcattc aacttggtga
      361 acattaaaga ttttcaaaag attgtgtggc cagtatctta cacaaggaga gatgaatgca
      421 aatgggctgg aaaagatatc ctgaaagaat gtgccaattt catcaaggtc ctggaggctt
      481 ataatcagac tcacttgtat gcctgtggaa ctggggcttt ccatccaatc tgcacctata
      541 ttgaagttgg acatcatcct gaggacaaca tttttaagct gcaggactca cattttgaaa
      601 acggtcgtgg gaagagccct tatgatccca aactactgac tgcctctctt ctaatagacg
      661 gtgagttgta ctctggaact gctgcggact tcatgggacg ggacttcgct atcttcagaa
      721 cactgggggа ccatcacccc atcaggacgg agcagcatga ctcccggtgg ctcaatgatc
      781 ctagattcat cagtgcccat ctcatcccag agagtgacaa ccctgaagat gacaaagtat
      841 atttttтctt ccgagaaaat gcaataggcg gagaacactc tggaaaagcc actcatgcta
      901 gaataggtca gatatgcaag aatgactttg gtggacacag aagtcttgtg aataaatgga
      961 caacattcct aaaagcacgc ctgatttgct ctgtgcccgg tcccaatggc attgacaccc
     1021 attttgatga attgcaggat gtattcctaa tgaactctaa agatcctaaa aatccgatcg
     1081 tctatggagt gttcacaaca tcaagcaaca tctttaaggg atctgctgtg tgcatgtaca
     1141 gcatgagtga tgtaagaagg gtgttccttg gtccatatgc tcacagagat ggtcccaact
     1201 atcagtgggt gccttaccaa ggaagagttc cttatccacg gccaggaact tgtcccagta
     1261 aaacatttgg cggatttgac tccacaaagg accttcctga tgatgtcata acttttggaa
     1321 gaagtcatcc agccatgtac aacccagtgt ttcctataaa taatcgcccg atcatgatca
     1381 aaacagatgt aaattatcag ttcacacaaa ttgttgtaga ccgagtggat gcagaagatg
     1441 gccagtatga tgttatgttc atcggaacag atgttggaac cgttcttaaa gtggtttcag
     1501 tccccaagga gacttggcat gacctagaag aagttcttct ggaagaaatg accgtcttcc
     1561 gggaaccaac aactatttcg gcaatggagc tttctactaa acagcaacag ctgtacattg
     1621 gctcaactgc gggagtggca cagcttcctc tacaccgctg tgacatctat ggcaaagcct
     1681 gtgcagaatg ctgcctcgct cgggaccctt actgtgcctg ggatgggtcc tcatgctcac
     1741 gctattttcc tactgcaaag aggcgcacaa gacgacaaga tataaggaat ggagacccac
     1801 tgactcactg ctctgacttg gaggaccatg ataatcatca tgggcccagc cttgaagaga
     1861 gaatcatcta tggagtggaa aacagtagta cattcttgga atgcagtccg aagtcacaga
     1921 gagccttggt atattggcaa tttcagagga gaaatcgaag atcgaaaaga gagatcagaa
     1981 tgggtgatca tatcatcagg acagaacaag ggctcctgct ccgtagcctg cagaagaagg
     2041 attcaggcaa ttacctgtgt cacgctgtgg aacacggatt catgcaaact cttcttaagg
     2101 taaccctgga agtcattgac acagaacatt tggaagaact tcttcataaa gatgacgatg
     2161 gagatggctc taagataaaa gaaatgtcga gcagcatgac gcccagccag aaagtctggt
     2221 accgagactt catgcagctc attaaccacc ccaacctgaa cacgatggat gagttctgtg
     2281 aacaagtgtg gaaaagggac cgaaagcaac gccgacaaag gccggggcac tctcaaggga
     2341 gcagcaacaa gtggaagcac atgcaagaga gcaagaaagg tagaaacagg aggacccacg
     2401 agtttgagcg ggcacccaga agtgtctgag ctgcgccacc tcccaaaacc tcaaacaagt
     2461 acaaacttgc ttagataata actggaaaaa atgcaataca catgaacatt tcatggcatt
     2521 atgtggatgt ttacaatgat gggaagttca accgggttcc accaatttaa gtccgtgagg
     2581 aactttccca gcaggctttc ttcagtatac caacgcttga cagagatcac aggtgagcat
     2641 agatgttcac gtccgctgac ttagtgtttc ctctgaaagt tcatattggt tccttctttg
     2701 cctgagaaat aaaaatgtca tttgccatcg aaaggagaaa aactgcatca gcaaagccat
     2761 tttattgaag caagagttga aaataaactg catggattta gtaagcagat gaatattcca
     2821 aaacgtgatt ggattcaagg atgttttggc taccagcact cgtgtttgta tgtactggag
     2881 aagtaaaata aggagaatga cactgagtga cat
//
```

Revised: October 24, 2001.

☐ **1:** W13166. ma93f11.r1 Soares...[gi:1287295] ProbeSet, Taxonomy, Traces, LinkOut

IDENTIFIERS

dbEST Id: **520223**
EST name: ma93f11.r1
GenBank Acc: W13166
GenBank gi: 1287295

CLONE INFO
Clone Id: IMAGE:318285 (5')
Source: IMAGE Consortium, LLNL
DNA type: cDNA

PRIMERS
Sequencing: ETPrimer
PolyA Tail: Unknown

SEQUENCE

GCCCTGAGTGTCATGTGTCTGGGCCTTGCCTGCTTGGGGTCCTGCAGAGCCAGGCCCAGG
ACTCAACTCAGAACTTGATCCCTGCCCCATCTCTGCTCACTGTCCCCCTGCAGCCAGACT
TCCGGAGCGATCAGTTCCGGGGCAGGTGGTACGTTGTGGGCCTGGCAGGCAATGCGGTCC
AGAAAAAAACAGAAGGCAGCTTTACGATGTACAGCACCATCTATGAGCTACAAGAGAACA
ATAGCTACAATGTCACCTCCATCCTGGTCAGGGACAGGACCAGGGCTGTCGCTACTGGAT
CAGAACATTTGTTCCAAGCTCCAGGGCTGGCCAGTTCACTCTGGGAAATATGCACAGGTA
TCCTCAGGTACAGAGCTACAATGTGCAAGTGGCCACACGGACTACAACCAGTTCGCCATG
GTATTTTTCCGAAAGACTTGTGAAAACAAGCAATACTTCAAAATTACGCTGTATGGAAGA
ACCAAGGAGCTGTCGCCTGAACTGAAGGAACGTTTCACCGCTTTGCCAAGTCTCTGGGCC
TCAAGGANGAGAACATCATGTTCTCGTGTCACGACGGACGAATGAATTGACACTTGAATT
GCGTGGTGAATGTGGCTGACTGGGAATCCCAGAGCACCAATGGTTCAGGCCGTGCTGGTC
TTGTGTGCGATCGCATGCTTCCTGGTGCCGAGAGACCACCTTGATGCGCCAGCAGCGGCA
TTCCGAGGTGCGGTTTTGAGCGCGTGTGAATTGTGCACAGCTCGCGCTACTTGCTGTAGA
CAGAAGTGGAGCCGTTGTGGTTGATAGTGTGGCCCGAGGAACATGTGAATTTGTGCGGGG
TGTCTCGTAGAGTGGGTATTTGTTTCGGAGCGTGTGAGACACGTGCGTGGGCACACGGTC
CTTCTCGTGGACCCTTTCAGTGTGGTAGAAGCCGTGGTATCGGCTCCGCAGTCTGGTGGC
GCGTCGTTCGGGCTTTCTAAGGAATTCGGCGGTGTGTCGTCTAAGCCTATAACGCGTGGA
TCTCTCCAAAGGTGGTCGAGTCTTGGGTTTTGTGAACGAGTTTTGGGTGACAAAAATGCG
CCGTGACACTCCTGGCGNNAGAGNGNGNGGGGTGGGGCGNGTGTGTGGTGGTGGGGGTGT
GGTGTGTGGTATGTGGGGGTCGCGGGGGTAGTGGGGCTGGCTGCGGTGTCGTGCGTGTGG
GTGCGTGGGGTGAGGGGTCCAGCGTGTGGTGGTGTGCGTATGTGTGTGTGAGGCGCGCGG
GGTGGATGCGTTGGTCGGCGTCGATCATGTGATGATGCGTGCGCGTGGTGGGTTGTAGTG
TTGTGGTGTGAGTA

Quality: High quality sequence stops at base: 423

Entry Created: Apr 26 1996
Last Updated: Oct 2 1997

COMMENTS

This clone is available royalty-free through LLNL ; contact the IMAGE Consortium (info@image.llnl.gov) for further information.
MGI: 208901

LIBRARY

Lib Name:	Soares mouse p3NMF19.5
Organism:	Mus musculus
Develop. stage:	19.5 dpc total fetus
Lab host:	DH10B (ampicillin resistant)
Vector:	pT7T3D (Pharmacia) with a modified polylinker
R. Site 1:	Not I
R. Site 2:	Eco RI
Description:	1st strand cDNA was primed with a Not I - oligo(dT) primer [5' TGTTACCAATCTGAAGTGGGAGCGGCCGCATTTTTTTTTTTTTTTTTT 3'], double-stranded cDNA was size selected, ligated to Eco RI adapters (Pharmacia), digested with Not I and cloned into the Not I and Eco RI sites of a modified pT7T3 vector (Pharmacia). Library went through one round of normalization to a Cot = 5. Library constructed by Bento Soares and M.Fatima Bonaldo. RNA was kindly provided by Dr. Minoru Ko (Wayne State University).

SUBMITTER

Name:	Marra M/Mouse EST Project
Lab:	WashU-HHMI Mouse EST Project
Institution:	Washington University School of MedicineP
Address:	4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
Tel:	314 286 1800
Fax:	314 286 1810
E-mail:	mouseest@watson.wustl.edu

CITATIONS

Title:	The WashU-HHMI Mouse EST Project
Authors:	Marra,M., Hillier,L., Allen,M., Bowles,M., Dietrich,N., Dubuque,T., Geisel,S., Kucaba,T., Lacy,M., Le,M., Martin,J., Morris,M., Schellenberg,K., Steptoe,M., Tan,F., Underwood,K., Moore,B., Theising,B., Wylie,T., Lennon,G., Soares,B., Wilson,R., Waterston,R.
Year:	1996
Status:	Unpublished

MAP DATA

Revised: October 24, 2001.

(FILE 'HOME' ENTERED AT 18:46:23 ON 03 MAY 2002)

FILE 'MEDLINE, BIOSIS, CANCERLIT, LIFESCI, BIOTECHDS' ENTERED AT 19:22:58
ON 03 MAY 2002

L1	241975	S	LYMPH(W)NODE#
L2	1812	S	HOMING(W)RECEPTOR#
L3	693	S	L1(S)L2
L4	156453	S	(DRUG# OR MULTIDRUG)(A)(RESISTAN?)
L5	0	S	L3(S)L4
L6	9	S	SERPIN(S)L4
L7	9	S	L6 AND PY<2001
L8	3		DUP REM L7 (6 DUPLICATES REMOVED)
L9	3378	S	EMT6 OR (EMT-6)
L10	498	S	L9 AND SARCOMA
L11	37	S	L9 AND PY<1975
L12	29		DUP REM L11 (8 DUPLICATES REMOVED)
L13	188	S	L9 AND (DRUG# OR MULTIDRUG)(A)RESISTAN?
L14	681	S	L9 AND HUMAN
L15	503	S	L9(S)HUMAN
L16	67	S	L15 AND L13
L17	60	S	L16 AND PY<2000
L18	26		DUP REM L17 (34 DUPLICATES REMOVED)

PAB,EPAB,DWPI
(semaphorin or (B adj 94) or (mel adj 14) or (mel-14) or 24p3 or proliferin or maspin) and ((drug or multidrug) adj
resistan$2)

S6494

JPAB,EPAB,DWPI
semaphorin or (B adj 94) or (mel adj 14) or (mel-14) or 24p3 or proliferin or maspin

S6493

USPT
((semaphorin or (B adj 94) or (mel adj 14) or (mel-14) or 24p3 or proliferin or maspin)with ((drug or multidrug) adj
resistan$2)) and @ad<19990131

S6492

USPT
(semaphorin or (B adj 94) or (mel adj 14) or (mel-14) or 24p3 or proliferin or maspin) with ((drug or multidrug) adj
resistan$2)

S6491

USPT
semaphorin or (B adj 94) or (mel adj 14) or (mel-14) or 24p3 or proliferin or maspin

S6490

JPAB,EPAB,DWPI
((((screen$3 or assay$3) with ((test adj compounds$1) or agent$1 or molecule$1))and ((drug or multidrug) adj
resistan$2))not us[pc]) and @pd<19990131

S6489

JPAB,EPAB,DWPI
(((screen$3 or assay$3) with ((test adj compounds$1) or agent$1 or molecule$1))and ((drug or multidrug) adj
resistan$2)) not us[pc]

S6488

JPAB,EPAB,DWPI
((screen$3 or assay$3) with ((test adj compounds$1) or agent$1 or molecule$1)) and ((drug or multidrug) adj

resistan$2)

S6487

JPAB,EPAB,DWPI
(screen$3 or assay$3) with ((test adj compounds$1) or agent$1 or molecule$1)

S6486

USPT
(((((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1))with ((drug or multidrug) adj resistan$2))and
@pradL54)or ((((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1))with ((drug or multidrug) adj
resistan$2))and @adL53)) not ((((((method$1 or assay$1) with ((test adj compounds$1) or agent$1 or molecule$1)
)with ((drug or multidrug) adj resistan$2))with (modulat$3 or decreas$3 or inhibit$3 or downregulat$3 or
antagoniz$3))and @pradL49)or (((((method$1 or assay$1) with ((test adj compounds$1) or agent$1 or
molecule$1))with ((drug or multidrug) adj resistan$2))with (modulat$3 or decreas$3 or inhibit$3 or downregulat$3
or antagoniz$3))and @adL48))

S6485

USPT
((((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1))with ((drug or multidrug) adj resistan$2))and
@pradL54) or ((((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1))with ((drug or multidrug) adj
resistan$2))and @adL53)

S6484

USPT
(((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1))with ((drug or multidrug) adj resistan$2)) and
@prad<19990131

S6483

USPT
(((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1))with ((drug or multidrug) adj resistan$2)) and
@ad<19990131

S6482

USPT

((screen$3) with ((test adj compounds$1) or agent$1 or molecule$1)) with ((drug or multidrug) adj resistan$2)

S6481

USPT

(screen$3) with ((test adj compounds$1) or agent$1 or molecule$1)

L28 ANSWER 33 OF 39 MEDLINE DUPLICATE 26
ACCESSION NUMBER: 87248074 MEDLINE
DOCUMENT NUMBER: 87248074 PubMed ID: 3596242
TITLE: Relationship between mitogen-regulated protein (MRP) and **proliferin** (PLF), a member of the prolactin/growth hormone family.
AUTHOR: Nilsen-Hamilton M; Hamilton R T; Alvarez-Azaustre E
CONTRACT NUMBER: CA39256 (NCI)
SOURCE: GENE, **(1987)** 51 (2-3) 163-70.
Journal code: FOP; 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198707
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870724

AB Mitogen-regulated protein (MRP) is a glycoprotein secreted by Swiss murine 3T3 cells whose levels are increased 63-fold or more over the controls by growth factors. The sequence of a 226-bp MRP cDNA clone showed that a region close to the C terminus of MRP is identical to a sequence found in the cDNA-encoding proliferin (PLF). PLF, cloned from Balb/c 3T3 cells, is a member of the prolactin/growth-hormone family. Here we show that MRP and PLF are also antigenically identical. Antiserum raised against purified MRP specifically immunoprecipitated PLF secreted by CV-1 cells that had been transfected with PLF cDNA in an SV40 vector. Also, fibroblast growth factor (FGF) specifically increased the amount of PLF poly(A)+ RNA in Swiss 3T3 cells. We have previously shown that FGF increases the amount of MRP and MRP mRNA synthesized by the same cells. The anti-MRP antiserum recognized both unglycosylated and glycosylated forms of MRP and PLF. The unglycosylated and glycosylated forms of PLF had the same Mr values as those of the unglycosylated (21,500) and glycosylated (34,000) forms of MRP. However, the anti-MRP antiserum did not recognize mouse prolactin and anti-mouse prolactin antibody did not recognize MRP. Evidently, MRP/PLF is an immunologically distinct member of the prolactin/growth-hormone family of secreted, intercellular regulators.

L28 ANSWER 34 OF 39 BIOSIS

L18 ANSWER 18 OF 26 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 92153685 MEDLINE
DOCUMENT NUMBER: 92153685 PubMed ID: 1346747
TITLE: Differential recognition of mdr1a and mdr1b gene products in **multidrug resistant** mouse tumour cell lines by different monoclonal antibodies.
AUTHOR: Barrand M A; Twentyman P R
CORPORATE SOURCE: MRC Clinical Oncology and Radiotherapeutics Unit, Cambridge, UK.
SOURCE: BRITISH JOURNAL OF CANCER, **(1992 Feb)** 65 (2) 239-45.
Journal code: AV4; 0370635. ISSN: 0007-0920.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920410
Last Updated on STN: 19970203
Entered Medline: 19920324

AB An immunocytochemical method was used to test the reactivity of the anti-P-glycoprotein antibodies, C219, MRK 16, JSB-1 and 265/F4 against **multidrug resistant** (MDR) variants derived from the **human** small cell lung carcinoma line, NCI-H69, the mouse fibrosarcoma line, RIF-1 and the mouse mammary tumour cell line, **EMT6**. C219 produced positive staining in MDR variants of both **human** and mouse tumour cell lines. MRK 16 and JSB-1 however recognised P-glycoprotein only in the **human** MDR cell lines and not in the mouse MDR cells. 265/F4 appeared the most selective of the monoclonal antibodies used, producing positive staining of MDR variants derived from the RIF-1 line, but not of MDR variants derived from the **EMT6** line. Total RNA was prepared from the mouse cell lines and, following reverse transcription, cDNA sequences were amplified by the polymerase chain reaction with primers specific for either the murine mdr1a or the mdr1b genes. From this it was possible to show that only the mdr1a gene is overexpressed in the resistant **EMT6** lines that do not stain with 265/F4 whereas both mdr1a and mdr1b are overexpressed in the positively staining resistant fibrosarcoma line, RIF/1.0. Low level expression of mdr1b was detected in the sensitive parent RIF-1 cells and increasing levels of expression correlated with increasing resistance in the lines, RIF/0.1, 0.2, 0.4 and 1.0. Expression of mdr1a was found only in the more resistant fibrosarcoma cell lines. It seems that 265/F4 recognises only the mdr1b P-glycoprotein. Western blotting confirmed that this antibody detects a 170 kDa protein only in membranes derived from the resistant fibrosarcoma cells. 265/F4 may thus be used to distinguish between the murine P-glycoprotein isoforms so revealing differences between tumour cell lines in cellular localisation and in the time of appearance of mdr1a and mdr1b P-glycoprotein following drug exposure.

L7 ANSWER 39 OF 141 CANCERLIT
ACCESSION NUMBER: 1998640215 CANCERLIT
DOCUMENT NUMBER: 98640215
TITLE: Diverse effects of tumor necrosis factor alpha on expression of the **multidrug resistance** -associated genes LRP and **MRP** (Meeting abstract).
AUTHOR: Stein U; Walther W; Laurencot C M; Scheffer G L; Scheper R J; Shoemaker R H
CORPORATE SOURCE: Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany 13122.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A3215.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199803

AB lt has previously been shown that treatment of multidrug resistant human tumor cells with cytokines can result in their sensitization towards drugs. Recently, we have reported that in vitro treatment of colon carcinoma cells with human tumor necrosis factor alpha (TNF) or transduction of the human TNF gene is associated with reduced expression of the mdr1 gene at the mRNA, protein and functional level. To investigate this phenomenon in relation to the more recently described MDR-associated genes LRP (lung resistance protein) and MRP (multidrug resistance associated protein), we evaluated the effect of TNF on the mRNA level by RT-PCR and on the protein level by immuno flow cytometry. Human colon carcinoma cell lines HCT15 and HCT116 were incubated with TNF for 2, 12, 24, 48 or 72 hours, or were transduced with the human TNF gene. **Modulated** expression of LRP and MRP was observed under both treatment conditions: LRP expression was reduced by TNF in an apparently time- and dose-related fashion. In contrast, MRP expression was increased on both expression levels. These results illustrate the complexity of multiple MDR phenotypes, which may coexist within a tumor cell population. They further suggest that strategies for **reversal** of MDR should not focus exclusively on the mdr1 gene, but should also address the net effect of MDR mechanisms which may respond in coordinate, or contrasting ways to **modulating** agents.

L7 ANSWER 49 OF 141 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:517083 BIOSIS
DOCUMENT NUMBER: PREV199799816286
TITLE: Altered expression of the genes regulating apoptosis in **multidrug resistant** human myeloid leukemia cell lines overexpressing MDR1 or **MRP** gene.
AUTHOR(S): Kim, Choong H.; Gollapudi, Sastry; Lee, Thomas; Gupta, Sudhir
CORPORATE SOURCE: Med. Sci. I, C-240 Univ. Calif., Irvine, CA 92697-4069 USA
SOURCE: International Journal of Oncology, (1997) Vol. 11, No. 5, pp. 945-950.
ISSN: 1019-6439.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Development of multidrug resistance (MDR) in cancer cells is associated with an overexpression of ATP-binding cassette proteins (e.g. P-glycoprotein (P-gp), multidrug resistance-associated protein (MRP)) and with **decreased** chemotherapeutic agent-induced apoptosis. In this study, we investigated whether MDR in cancer cells was associated with altered expression of genes regulating apoptosis using a drug sensitive human myeloid leukemia cell line (HL60), and its MDR sublines, overexpressing MRP (HL60/AR) or P-gp (HL60/taxol). Expression of apoptotic genes was examined at the protein level by flow cytometry and at the mRNA level by **reverse** transcriptase-polymerase chain reaction (RT-PCR). We observed that the MDR cells either did not express or expressed a reduced level of the apoptosis promoters Fas, Bcl-x-s, and Bax, whereas expression of the apoptosis repressor Bcl-x-L was increased. Both vincristine and anti-Fas monoclonal antibody induced apoptosis in HL60 cells but failed to do so in both MDR cell lines. These data suggest that acquired MDR in cancer cells, regardless of the type of overexpressed ABC transporter, may be associated with increased expression of antiapoptotic genes and **decreased** expression of pro-apoptotic genes.

order

L7 ANSWER 47 OF 141 MEDLINE DUPLICATE 28
ACCESSION NUMBER: 1998019056 MEDLINE
DOCUMENT NUMBER: 98019056 PubMed ID: 9358024
TITLE: Retrovirus-mediated gene transfer of the **multidrug resistance**-associated protein (**MRP**) cDNA protects cells from chemotherapeutic agents.
AUTHOR: D'Hondt V; Caruso M; Bank A
CORPORATE SOURCE: Department of Medicine, Columbia University, College of Physicians and Surgeons, New York, NY 10032, USA.
SOURCE: HUMAN GENE THERAPY, **(1997 Oct 10)** 8 (15) 1745-51.
Journal code: A12; 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19980217
Entered Medline: 19980203

AB Transduction of hematopoietic progenitors with a multidrug resistance gene like mdr-1 or mrp aims to protect bone marrow from toxicity of chemotherapeutic agents. The interest in the use of mrp as an alternative to mdr-1 gene transfer for bone marrow protection lies in its different **modulation**. Indeed, classical P-gp **reversal** agents, tested in the clinic to **decrease** mdr-1 tumor resistance, have little or no effect on MRP function. This would allow, in the same patient, the use of **reversal** agents to **decrease** P-gp tumor resistance without **reversing** bone marrow protection of the transduced hematopoietic cells provided by multidrug resistance-associated protein (MRP). As a first step, we have constructed and tested two different mrp-containing vectors with either the Harvey retroviral long terminal repeat (LTR) or PGK as promoters and generated ecotropic producer cells. We have shown by Southern blot analysis that retroviral supernatant from these producer cells can efficiently transmit the mrp gene to target cells. Mrp expression could be detected by fluorescence-activated cell sorting (FACS) analysis in the producer cells. The transduced cells have increased resistance to doxorubicin, vincristine, and etoposide. Furthermore, chemoprotection of the transduced cells was increased after selection with chemotherapeutic agents in the presence of glutathione, a co-factor for MRP function. These data indicate that mrp retroviral vectors may be useful for chemoprotection and selection.

motivation for upregulation

L7 ANSWER 45 OF 141 CANCERLIT
ACCESSION NUMBER: 1998639569 CANCERLIT
DOCUMENT NUMBER: 98639569
TITLE: Chemoprotection by retroviral gene transfer of the **multidrug resistance**-associated protein (**MRP**) cDNA (Meeting abstract).
AUTHOR: D'Hondt V; Machiels J P; Caruso M; Bank A; Symann M
CORPORATE SOURCE: Universite Catholique de Louvain, Brussels, Belgium 1200.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A2569.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199801

AB The interest in the use of MRP as an alternative to mdr-1 gene transfer for bone marrow protection lies in its different **modulation**. Classical P-gp **reversal** agents, tested in clinic to **decrease** mdr-1 tumor resistance, have little or no effect on MRP function. This would allow, in the same patient, the use of **reversal** agents to **decrease** mdr-1 tumor resistance without **reversing** bone marrow protection of the transduced hematopoietic cells provided by MRP. We have constructed two MRP-containing retroviral vectors and generated producer cells and have shown by Southern blot analysis that retroviral supernatant from these producer cells can efficiently transmit the MRP gene to target cells. MRP expression was detected by FACS analysis in the producer cells as in the transduced cells, conferring multidrug resistance to both. Furthermore, selection of transduced cells in chemotherapeutic drug was achieved. These data indicate that MRP retroviral vectors have a potential application for bone marrow chemoprotection. We are now developing a murine and an in vitro human model to test this hypothesis.

L7 ANSWER 63 OF 141 CANCERLIT
ACCESSION NUMBER: 97619095 CANCERLIT
DOCUMENT NUMBER: 97619095
TITLE: Role of **multidrug resistance** protein (**MRP**)-mediated transport of chlorambucil and melphalan conjugated to glutathione in **drug resistance** (Meeting abstract).
AUTHOR: Barnouin K; Leier I; Jedlitschky G; Pourtier-Manzanedo A; Konig J; Keppler D
CORPORATE SOURCE: Division of Tumor Biochemistry, Deutsches Krebsforschungszentrum, D-69120 Heidelberg, Germany.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A408.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199709

AB The human multidrug resistance protein (MRP) confers resistance to a number of different cytostatic drugs and functions as an export pump for glutathione S-conjugates, glucuronides, and other amphiphilic anions. The present study details for the first time MRP-mediated ATP-dependent transport of various glutathione S-conjugates of the alkylating agents chlorambucil and melphalan. In membrane vesicles from MRP-transfected HeLa cells transport rates of the conjugates **decreased** in the following order: monoglutathionyl chlorambucil, diglutathionyl chlorambucil, and monohydroxy monoglutathionyl chlorambucil; and monoglutathionyl melphalan and monohydroxy monoglutathionyl melphalan. Immunoblotting with a polyclonal antibody directed against the carboxyl-terminal sequence of human MRP indicated the presence of the hamster homolog of MRP in the membranes of normal and glutathione transferase alpha-overexpressing chlorambucil-resistant Chinese Hamster Ovary (CHO) cells. This was confirmed by amplification and sequencing of a fragment of hamster mrp cDNA. In membrane vesicles prepared from both CHO cell lines we observed ATP-dependent transport of monoglutathionyl chlorambucil and of the glutathione S-conjugate leukotriene C4, a high-affinity substrate of MRP. Comparison of chlorambucil cytotoxicity in a number of MRP-overexpressing and parental cells, as well as in chlorambucil-resistant and control CHO cells, demonstrated that MRP expression alone is not sufficient to confer resistance to the alkylating drug and that its conjugation to glutathione is of additional importance.

L7 ANSWER 64 OF 141 MEDLINE DUPLICATE 37

L7 ANSWER 73 OF 141 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 1996-04511 BIOTECHDS
TITLE: **Multidrug-resistance** protein **MRP** and DNA encoding it; recombinant multidrug-resistance-associated protein production using new vector and sense and antisense DNA sequence potential application in small cell lung carcinoma gene therapy
AUTHOR: Deerley R G; Cole S P C
PATENT ASSIGNEE: Univ.Kingston-Queen's
LOCATION: Kingston, Canada.
PATENT INFO: US 5489519 **6 Feb 1996**
APPLICATION INFO: US 1993-141893 26 Oct 1993
PRIORITY INFO: US 1993-141893 26 Oct 1993
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1996-115615 [12]
AN 1996-04511 BIOTECHDS
AB An isolated nucleic acid (I) comprising a nucleotide sequence encoding a multidrug-resistance-associated protein (MRP) having at least 70% homology to the protein sequence disclosed is claimed. The MRP is resistant to doxorubicin, on a drug-sensitive mammal cell when the protein is expressed in the cell and the resistance is not **reversed** by chemosensitizers which **reverse** P-glycoprotein-mediated multidrug-resistance. Also claimed are: a naturally-occurring nucleic acid which hybridizes under stringent conditions to (I) and encodes a protein having activity of the MRP with at least 60% homology to the disclosed protein sequence; isolated nucleic acid conferring multidrug-resistance on a cell; antisense (I); a recombinant expression vector containing (I); a transformed host; preparation of a MRP involving culturing a transformant in suitable medium and recovering the product; and a diagnostic kit for multidrug-resistant tumor cells comprising a DNA probe complementary to (I). The sense and antisense nucleic acid can be used in small cell lung carcinoma gene therapy, especially following chemotherapy. (49pp)

L7 ANSWER 74 OF 141 CANCERLIT

L7 ANSWER 19 OF 141 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 1999120323 MEDLINE
DOCUMENT NUMBER: 99120323 PubMed ID: 9923448
TITLE: Selectively induced high **MRP** gene expression in **multidrug-resistant** human HL60 leukemia cells.
AUTHOR: Wada H; Saikawa Y; Niida Y; Nishimura R; Noguchi T; Matsukawa H; Ichihara T; Koizumi S
CORPORATE SOURCE: Department of Pediatrics, Kanazawa University School of Medicine, Japan.
SOURCE: EXPERIMENTAL HEMATOLOGY, **(1999 Jan)** 27 (1) 99-109.
Journal code: EPR; 0402313. ISSN: 0301-472X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990225

AB A subclone HL60/DOX was selected from a human leukemic HL60 cell line for resistance to doxorubicin (DOX) by exposure to stepwise increasing concentrations of the drug and coexposure to a potential P-glycoprotein (P-gp) inhibitor, cepharanthine (a biscoclaurine alkaloid). Compared with the parent HL60 cells, the HL60/DOX cells were 13.0-fold more resistant to DOX and showed multidrug-resistant (MDR) phenotype characterized by 4.6-fold, 2.3-fold, and 5.7-fold cross-resistance to vincristine, pirarubicin, and etoposide, respectively, but no cross-resistance to alkylating agent, cisplatin. Immunocytochemical analyses using the specific monoclonal antibody, MRPr1, and quantitative analyses using a competitive **reverse** transcription-polymerase chain reaction (CRT-PCR) confirmed overexpression of MRP gene products (about 8-fold determined by CRT-PCR) in this resistant clone. The P-gp expression was not detectable by the monoclonal antibody, C219, in the HL60/DOX cells, and that was consistent with extremely low levels of mdr1 mRNA expression determined by CRT-PCR in this clone. Drug accumulation and efflux studies demonstrated the significantly increased efflux rate of DOX compared to the parent HL60 cells. This enhancement of DOX efflux was **reversed** by the addition of 10 microM verapamil. To investigate the additional underlying mechanisms contributing to MDR phenotype in the HL60/DOX cells, the levels of DNA topoisomerases (Topo) including Topo I, Topo IIalpha, and Topo IIbeta, and gamma-glutamylcystein synthetase (y-GCS) expression were determined using CRT-PCR techniques. Normal expression of each enzyme at the transcriptional level was demonstrated in this resistant clone. Southern blot analysis of the gene organization in the HL60/DOX cells revealed the amplification of MRP gene. These results indicate that alteration of the drug accumulation from enhanced efflux appears to be a major mechanism(s) of MDR phenotype and attributable to high levels of MRP expression in the HL60/DOX cells. Overexpression of MRP in this clone is regulated by the genomic amplification of DNA and increased levels of the MRP mRNA, independently with the normal expression of Topo I, Topo IIalpha, Topo IIbeta, or gamma-GCS.

L7 ANSWER 140 OF 141 CANCERLIT
ACCESSION NUMBER: 95612433 CANCERLIT
DOCUMENT NUMBER: 95612433
TITLE: ATP-dependent glutathione conjugate transport in HL60 cells
overexpressing the **multidrug resistance** associated protein (**MRP**) (Meeting abstract).
AUTHOR: Jedlitschky G; Leier I; Buchholz U; Barnouin K; Center M; Keppler D
CORPORATE SOURCE: Division of Tumor Biochemistry, Deutsches Krebsforschungszentrum, 69120 Heidelberg, Germany.
SOURCE: Anticancer Drugs, **(1994)**. Vol. 5, Suppl. 1, pp. 4.
ISSN: 0959-4973.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199510

AB ATP-dependent transport of the glutathione conjugate leukotriene C4 (LTC4) was studied in membrane vesicles from the human leukemia cell line HL60 and a subline isolated for resistance to adriamycin (HL60/ADR) which was shown to overexpress a 190-kD glycoprotein encoded by the MRP gene. The function of this ATP-binding protein, which has a limited sequence similarity with P-glycoproteins, is so far unknown. The rate of ATP-dependent LTC4 transport observed in membrane vesicles prepared from the HL60/ADR cells was more than 25-fold higher than in membrane vesicles from parent HL60 cells (25 pmol x mg protein-1 x min-1 vs less than 1 pmol x mg protein-1 x min-1). In photoaffinity labeling studies with these membranes a LTC4-binding protein of about 190 kD was detected only in the HL60/ADR membranes. The quinoline-based leukotriene receptor **antagonist** MK 571 completely inhibited the ATP-dependent LTC4 transport by HL60/ADR membrane vesicles at a concentration of 5 uM. The [3H]LTC4 labeling of the 190 kD glycoprotein was also competed for by this transport inhibitor. These data indicate that P-gp-independent, p190-mediated multidrug resistance is associated with an enhanced ATP-dependent transport of glutathione conjugates.

L7 ANSWER 141 OF 141 CANCERLIT

L7 ANSWER 139 OF 141 CANCERLIT
ACCESSION NUMBER: 95612480 CANCERLIT
DOCUMENT NUMBER: 95612480
TITLE: **Reversal** of **drug resistance** in **MRP** overexpressing **multidrug resistant** human lung tumor cells (Meeting abstract).
AUTHOR: Versantvoort C H; Broxterman H J; Bagrij T; Twentyman P R
CORPORATE SOURCE: MRC Clinical Oncology and Radiotherapeutics Unit, Hills Road, Cambridge CB2 2QH, UK.
SOURCE: Anticancer Drugs, **(1994)**. Vol. 5, Suppl. 1, pp. 30.
ISSN: 0959-4973.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199510

AB A number of multidrug resistant (MDR) tumor cell lines, which do not overexpress P-glycoprotein, have now been reported to overexpress the MRP gene. In most of these MRP overexpressing resistant cell lines the accumulation of drugs is **decreased** as a result of an enhanced drug efflux. In this study, we examined the effects of buthionine sulfoximine (BSO), an inhibitor of glutathione synthesis, on drug resistance and cellular drug accumulation in two, doxorubicin-selected, MRP overexpressing, MDR human lung cancer cell lines. The COR-L23/R cells were 21-, 32- and 21-fold resistant to daunorubicin, vincristine and rhodamine 123, respectively, as measured in a 5-day MTT assay. Pretreatment of the resistant cells with BSO (25 uM, 20 h) enhanced the toxicity of the drugs 10-, 18- and 18-fold. Moreover, pretreatment of the resistant cells with BSO increased the cellular accumulation and retention of daunorubicin and rhodamine up to the level of the parental COR-L23/P cells, while having no effect on the parental cells. In another MRP overexpressing MDR cell line, GLC4/ADR, **reversal** of daunorubicin toxicity by BSO was also associated with a complete **reversal** of the accumulation deficit. Total glutathione content was lower in the COR-L23/R cells than in the parental cells 11.2 and 18.6 nmol/10(6) cells, respectively. However, in the GLC4/ADR cells the glutathione content was higher than in the GLC4 cells, 9.5 vs 5.1 nmol/10(6) cells. The glutathione content was reduced by exposure to BSO: 2- to 3-fold in the CORL23 cell lines and 3- to 5-fold in the GLC4 cell lines. When intermediate levels of glutathione (40-70% of control) were obtained, only a partial **reversal** of the daunorubicin accumulation deficit was measured in the resistant cells. Thus, BSO enhances the toxicity of drugs in the MRP overexpressing MDR cells by inhibition of the enhanced efflux. The possible involvement of cellular glutathione in drug transport in MRP overexpressing MDR cell lines is currently being investigated.

L7 ANSWER 140 OF 141 CANCERLIT

L7 ANSWER 129 OF 141 MEDLINE DUPLICATE 74
ACCESSION NUMBER: 95118326 MEDLINE
DOCUMENT NUMBER: 95118326 PubMed ID: 7818510
TITLE: The specific bisindolylmaleimide PKC-inhibitor GF 109203X efficiently **modulates MRP**-associated multiple **drug resistance**.
AUTHOR: Gekeler V; Boer R; Ise W; Sanders K H; Schachtele C; Beck J
CORPORATE SOURCE: Byk Gulden, Konstanz, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1995 Jan 5)** 206 (1) 119-26.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950217
Last Updated on STN: 19990129
Entered Medline: 19950209

AB The newly identified drug transporter MRP is functionally linked to a multiple drug resistance independent from P-glycoprotein. Resistance modifiers for this type of MDR are rare at present. We analyzed the **modulating** effect of the highly selective bisindolylmaleimide PKC inhibitor GF 109203X on the MRP overexpressing human MDR sublines HL60/AR and GLC4/ADR. Applying a 72 hour MTT-assay we demonstrate a complete **reversal** of the vincristine resistance of HL60/AR cells. Adriamycin resistance of HL60/AR, or vincristine resistance of GLC4/ADR were partially **reversed**. Furthermore, rhodamine 123 efflux from HL60/AR was strongly **modulated** by GF 109203X. Since the PKC inhibitor did not significantly influence MRP gene expression at the mRNA level which was examined by cDNA-PCR, our results suggest either a direct interaction of the compound with MRP or/and an indirect influence on MRP activity via altering the phosphorylation status of the transporter.

L7 ANSWER 130 OF 141 MEDLINE DUPLICATE 7

L7 ANSWER 128 OF 141 MEDLINE DUPLICATE 73
ACCESSION NUMBER: 96034538 MEDLINE
DOCUMENT NUMBER: 96034538 PubMed ID: 8534927
TITLE: Difloxacin **reverses multidrug resistance** in HL-60/AR cells that overexpress the **multidrug resistance**-related protein (**MRP**) gene.
AUTHOR: Gollapudi S; Thadepalli F; Kim C H; Gupta S
CORPORATE SOURCE: Division of Basic and Clinical Immunology, University of California, Irvine 92717, USA.
SOURCE: ONCOLOGY RESEARCH, **(1995)** 7 (5) 213-25.
Journal code: BBN; 9208097. ISSN: 0965-0407.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960221
Last Updated on STN: 19970203
Entered Medline: 19960208

AB In this study, we have examined the in vitro chemosensitizing activity of difloxacin, a quinolone antimicrobial agent, in the multidrug-resistant human myeloid leukemia HL-60/AR cell line. HL-60/AR cells were found to overexpress multidrug resistance-associated protein (MRP) mRNA as compared to HL-60 cells. Difloxacin, in a concentration-dependent manner, increased the sensitivity of HL-60/AR cells to daunorubicin, adriamycin, and vincristine, and partially corrected the altered drug transport. In addition, difloxacin corrected subcellular distribution of adriamycin by inducing redistribution of the drug from the perinuclear region to the nucleus in HL-60/AR cells. The chemosensitizing effect of difloxacin was observed at clinically achievable concentrations. We conclude that difloxacin is an effective chemosensitizer of MRP-associated multidrug-resistant tumor cells and is a potential candidate for clinical use to **reverse** multidrug resistance.

L7 ANSWER 126 OF 141 MEDLINE DUPLICATE 72

ACCESSION NUMBER: 95272127 MEDLINE
DOCUMENT NUMBER: 95272127 PubMed ID: 7752673
TITLE: **Drug resistance** mechanisms and **MRP** expression in response to epirubicin treatment in a human leukaemia cell line.
AUTHOR: Davey R A; Longhurst T J; Davey M W; Belov L; Harvie R M; Hancox D; Wheeler H
CORPORATE SOURCE: Bill Walsh Cancer Research Laboratories, Department of Clinical Oncology, Royal North Shore Hospital, St. Leonards, Australia.
SOURCE: LEUKEMIA RESEARCH, **(1995 Apr)** 19 (4) 275-82.
Journal code: K9M; 7706787. ISSN: 0145-2126.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 19950629
Entered Medline: 19950622

AB A drug resistant series of sublines were developed by treating the human leukaemia CCRF-CEM cell line with 16-1000 ng/ml of the anthracycline, epirubicin. The sublines developed resistance in two stages, neither involving detectable levels of P-glycoprotein. Treatment with up to 50 ng/ml epirubicin produced sublines with cross resistance limited to the anthracyclines and etoposide. Treatment with 100-1000 ng/ml epirubicin produced sublines with increased expression of the mrp gene, increased resistance to the anthracyclines and etoposide, additional cross resistance to vincristine and colchicine, **decreased** drug accumulation and **reversal** of resistance by verapamil and by buthionine sulphoximine (BSO; an inhibitor of glutathione synthesis). Our results indicate an interaction between MRP and glutathione metabolism as a mechanism for multidrug resistance.

L7 ANSWER 124 OF 141 MEDLINE DUPLICATE 70
ACCESSION NUMBER: 95194429 MEDLINE
DOCUMENT NUMBER: 95194429 PubMed ID: 7887949
TITLE: The leukotriene LTD4 receptor **antagonist** MK571 specifically **modulates MRP** associated **multidrug resistance.**
AUTHOR: Gekeler V; Ise W; Sanders K H; Ulrich W R; Beck J
CORPORATE SOURCE: Byk Gulden, Konstanz, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1995 Mar 8)** 208 (1) 345-52.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950425
Last Updated on STN: 19970203
Entered Medline: 19950413

AB The multidrug resistant cell lines HL60/AR and GLC4/ADR show high overexpression of the gene encoding the multidrug resistance associated protein MRP compared to their drug sensitive parental counterparts. This and the virtual absence of mdr1/P-glycoprotein gene expression was proven by a complementary DNA polymerase chain reaction (cDNA-PCR) approach. Applying a 72-hour tetrazolium based colorimetric MTT-assay we demonstrate on both MDR sublines a dose-dependent **modulation** of drug resistances by the leukotriene LTD4 receptor **antagonist** MK571. A complete **reversal** of vincristine resistances was achieved at final MK571 concentrations of 30 microM (HL60/AR) or 50 microM (GLC4/ADR) which by itself did not disturb cellular proliferation. The drug resistance of a mdr1/P-gp overexpressing multidrug-resistant HL60 subline, in contrast, was not significantly affected by MK571. Similar effects were seen using the glutathione (GSH) synthesis inhibitor buthionine sulfoximine (BSO). Our results point to a relationship between MRP and a conjugate transporter and identify MK571 as a new tool structure for developing **modulators** specific for a MRP associated multidrug resistance.

L7 ANSWER 122 OF 141 MEDLINE DUPLICATE 68
ACCESSION NUMBER: 95367497 MEDLINE
DOCUMENT NUMBER: 95367497 PubMed ID: 7640227
TITLE: Chemosensitisation of spontaneous **multidrug resistance** by a 1,4-dihydropyridine analogue and verapamil in human glioma cell lines overexpressing **MRP** or MDR1.
AUTHOR: Abe T; Koike K; Ohga T; Kubo T; Wada M; Kohno K; Mori T; Hidaka K; Kuwano M
CORPORATE SOURCE: Department of Biochemistry, Kyushu University School of Medicine, Fukuoka, Japan.
SOURCE: BRITISH JOURNAL OF CANCER, **(1995 Aug)** 72 (2) 418-23.
Journal code: AV4; 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19980206
Entered Medline: 19950921

AB Multidrug resistance phenotypes in human tumours are associated with the overexpression of the 170 kDa P-glycoprotein encoded by the multidrug resistance 1 (MDR1) gene, and also with that of the non-P-glycoprotein-mediated multidrug resistance gene, MRP, which encodes a 190 kDa membrane ATP-binding protein. We have previously reported that overexpression of MRP appears to be responsible for spontaneous multidrug resistance in some human glioma cell lines (Abe et al., Int. J. Cancer, 58, 860-864, 1994). In this study, we investigated whether chemosensitising agents of P-glycoprotein-mediated multidrug resistance such as verapamil, a biscoclaurine alkaloid (cepharanthine), and a dihydropyridine analogue (NIK250) could also **reverse** multidrug resistance in human glioma cells. The glioma cell lines were the two MRP-expressing cell lines, T98G and IN500, an MDR1-expressing cell line, CCF-STTG1, and the MRP1 MDR1-non-expressing cell line, IN157. Verapamil and NIK250 almost completely **reversed** drug resistance to vincristine, etoposide and doxorubicin in T98G cells, while they also **reversed** drug resistance to vincristine and etoposide, but only partially to doxorubicin in IN500 cells. Cepharanthine as well as verapamil and NIK250 **reversed** vincristine resistance in CCF-STTG1 cells, but cepharanthine only partially **reversed** drug resistance in T98G and IN500 cells. The cellular accumulation of [3H]etoposide increased about 2- and 3-fold compared with control in T98G cells in the presence of verapamil and NIK250 respectively. Furthermore, the release of doxorubicin from the nuclei of T98G cells was blocked by NIK250. However, NIK250 and verapamil caused no apparent increase in vincristine accumulation in T98G cells. NIK250 or verapamil might exert inhibitory effects upon MRP function, resulting in a **reversal** of MRP-mediated spontaneous multidrug resistance in cultured human glioma cells.

L7 ANSWER 122 OF 141 MEDLINE DUPLICATE 68
ACCESSION NUMBER: 95367497 MEDLINE
DOCUMENT NUMBER: 95367497 PubMed ID: 7640227
TITLE: Chemosensitisation of spontaneous **multidrug resistance** by a 1,4-dihydropyridine analogue and verapamil in human glioma cell lines overexpressing **MRP** or MDR1.
AUTHOR: Abe T; Koike K; Ohga T; Kubo T; Wada M; Kohno K; Mori T; Hidaka K; Kuwano M
CORPORATE SOURCE: Department of Biochemistry, Kyushu University School of Medicine, Fukuoka, Japan.
SOURCE: BRITISH JOURNAL OF CANCER, **(1995 Aug)** 72 (2) 418-23.
Journal code: AV4; 0370635. ISSN: 0007-0920.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 19950930
Last Updated on STN: 19980206
Entered Medline: 19950921

AB Multidrug resistance phenotypes in human tumours are associated with the overexpression of the 170 kDa P-glycoprotein encoded by the multidrug resistance 1 (MDR1) gene, and also with that of the non-P-glycoprotein-mediated multidrug resistance gene, MRP, which encodes a 190 kDa membrane ATP-binding protein. We have previously reported that overexpression of MRP appears to be responsible for spontaneous multidrug resistance in some human glioma cell lines (Abe et al., Int. J. Cancer, 58, 860-864, 1994). In this study, we investigated whether chemosensitising agents of P-glycoprotein-mediated multidrug resistance such as verapamil, a biscoclaurine alkaloid (cepharanthine), and a dihydropyridine analogue (NIK250) could also **reverse** multidrug resistance in human glioma cells. The glioma cell lines were the two MRP-expressing cell lines, T98G and IN500, an MDR1-expressing cell line, CCF-STTG1, and the MRP1 MDR1-non-expressing cell line, IN157. Verapamil and NIK250 almost completely **reversed** drug resistance to vincristine, etoposide and doxorubicin in T98G cells, while they also **reversed** drug resistance to vincristine and etoposide, but only partially to doxorubicin in IN500 cells. Cepharanthine as well as verapamil and NIK250 **reversed** vincristine resistance in CCF-STTG1 cells, but cepharanthine only partially **reversed** drug resistance in T98G and IN500 cells. The cellular accumulation of [3H]etoposide increased about 2- and 3-fold compared with control in T98G cells in the presence of verapamil and NIK250 respectively. Furthermore, the release of doxorubicin from the nuclei of T98G cells was blocked by NIK250. However, NIK250 and verapamil caused no apparent increase in vincristine accumulation in T98G cells. NIK250 or verapamil might exert inhibitory effects upon MRP function, resulting in a **reversal** of MRP-mediated spontaneous multidrug resistance in cultured human glioma cells.

L7 ANSWER 114 OF 141 CANCERLIT
ACCESSION NUMBER: 97609782 CANCERLIT
DOCUMENT NUMBER: 97609782
TITLE: Probenecid **reverses multidrug resistance** in tumor cells that overexpress **multidrug resistance**-related protein (**MRP**) gene and not in tumor cells that overexpress **multidrug resistance** 1 (MDR 1) gene (Meeting abstract).
AUTHOR: Gupta S; Gollapudi S
CORPORATE SOURCE: University of California, Irvine, CA 92717.
SOURCE: Int J Oncol, **(1995)**. Vol. 7, Suppl., pp. 987. ISSN: 1019-6439.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199705

AB Objective and Rationale: The development of multidrug resistance (MDR) to anticancer agents by tumor cells is a major concern to the therapeutic cure of cancer. An overexpression of MDR 1 and its product P-glycoprotein (P-gp), a member of ATP-binding cassette (ABC) transport proteins, is associated with MDR and a number of agents are available that **reverse** MDR in MDR 1 overexpressing tumor cells. However, there are MDR tumor cells that lack MDR 1 but overexpress MRP gene (another member of ABC transport protein). Currently there is a need for agents that can **reverse** MDR in tumor cell lines that overexpress MRP gene and its product. Because MRP facilitates transport of leukotriene C4 (LTC4), and probenecid is an inhibitor of LTC4, we investigated the effect of probenecid on drug sensitivity, drug accumulation, subcellular drug distribution and intracellular pH (pHi) in human myeloid leukemia HL60/AR MDR cell line that overexpresses MRP gene and its product. Methods: Drug sensitivity was tested by MTT assay. Intracellular accumulation of daunorubicin (DNR) and vincristine (VCR) was measured by flow cytometry and scintillation counter respectively. Intracellular pH was assessed with BCECF-AM dye, using FACScan. Subcellular drug distribution was analyzed with laser-based confocal microscope. Results: Probenecid, in a concentration dependent manner, **reversed** resistance to daunorubicin (DNR) and vincristine (VCR). However, probenecid had no effect on drug (DNR and VCR) accumulation, subcellular drug distribution and pHi. The concentrations of probenecid that **reversed** multidrug resistance are clinically achievable in vivo. In contrast, probenecid did not **reverse** MDR in P-gP overexpressing murine leukemia P388/ADR cell line. Conclusion: These data suggest that probenecid is an effective chemosensitizer of MRP-associated multidrug resistant tumor cells and is a potential candidate for clinical use to **reverse** MDR.

L7 ANSWER 112 OF 141 CANCERLIT
ACCESSION NUMBER: 96649455 CANCERLIT
DOCUMENT NUMBER: 96649455
TITLE: Protein kinase inhibitor-induced alterations of drug uptake
and surface antigen expression in human **multidrug resistant**, Pgp and non-Pgp (**mrp**) promyelocytic leukemia (HL-60) cells (Meeting abstract).
AUTHOR: Sedlak J; Hunakova L; Sulikova M; Pailingerova D; Chorvath B
CORPORATE SOURCE: Cancer Research Institute, SAS, Spitalska 21, SK-812 32 Bratislava, Slovak Republic.
SOURCE: Anticancer Res, **(1995)**. Vol. 15, No. 5A, pp. 1644.
ISSN: 0250-7005.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199608

AB Protein kinase inhibitors staurosporine and CGP 41 251--a benzoylated derivative of staurosporine with selective PRC inhibitory activity, **reversed** the **decreased** daunomycine and rhodamine R123 uptake in MDR-1 (HL-60/VCR) but not in MRP (HL-60/ADR) cells. CGP 41 251 **reversed** the **decreased** daunomycin uptake in HL-60/VCR cells (with Pgp-mediated drug resistance) more efficiently (as compared on the equimolar basis) than staurosporine. The protein tyrosine kinase inhibitor genistein unexpectedly **modulated** the **decreased** daunomycin uptake in Pgp-positive (HL60/VCR) cells, but not in HL-60/ADM (MRP) cells. Cell surface phenotype of two HL-60 drug resistant cell sublines, ie, HL-60/VCR (MDR1) and HL-60/ADR (MRP), were compared with that of the parental, drug-sensitive HL-60 cells. Both drug-resistant cell lines expressed markedly **decreased** levels of cell surface HLA class I antigen in comparison with the parental, drug sensitive HL-60 cells. Interferon-gamma induced a marked HLA class I upregulation in both examined drug-resistant HL-60 cell lines and, to a lesser extent, also in their parental, drug-sensitive HL-60 cells. Both studied protein kinase inhibitors (staurosporine and CGP 41 251) exhibited variable effects on cell surface antigen (HLA, ICAM-1, CD59) expression, suggesting complex interactions between PKC-dependent and independent mechanisms in the regulation of surface antigen expression in these cell lines.

L7 ANSWER 106 OF 141 CANCERLIT
ACCESSION NUMBER: 95609981 CANCERLIT
DOCUMENT NUMBER: 95609981
TITLE: Ethoxylated fatty acids (EOFAs), active components contained in Cremophor EL, enhance daunorubicin (dnr) accumulation in P-glycoprotein (Pgp) but not **multidrug resistance**-associated protein (**MRP**) overexpressing cells (Meeting abstract).
AUTHOR: Tong Y; Piraner O N; Doyle L A; Cornblatt B; Chang B; Yang W; Ross D D
CORPORATE SOURCE: Univ. of Maryland Cancer Center, Baltimore, MD 21201.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1995)**. Vol. 36, pp. A2206.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199508

AB Three EOFAs were synthesized with structural similarities to active multidrug resistance (MDR) **modulating** EOFAs identified in Cremophor EL. These EOFAs were tested for their effects on dnr accumulation (1 ug/ml, 3 hr) in MDR sublines of human leukemia HL-60 cells that overexpress Pgp (HL-60/Vinc) or MRP (HL-60/AR). In HL-60/Vinc cells, the EOFAs caused a dose-dependent enhancement of intracellular dnr content (measured by flow cytometry), with maximal enhancement (Emax) attained at 10 ug/ml. This represents a 15- to 50-fold enhancement in potency, compared to the effects of Cremophor EL on HL60/Vinc cells. The level of intracellular dnr accumulation attained at Emax for HL60/Vinc cells was equal that of parental, drug-sensitive HL-60 cells. In contrast, concentrations of EOFAs up to 100 ug/ml produced enhancement of dnr accumulation in HL-60/AR cells that were only 20% to 50% those attained in parental HL-60 cells. This is similar to the response to Cremophor EL in these cells, where only slight enhancement of dnr accumulation was observed. Paradoxically, HL-60/AR cells were, in general, more sensitive to the cytotoxic effects of the EOFAs than were HL-60/Vinc or HL-60 cells. The increased potency of these EOFAs over Cremophor EL in enhancing dnr accumulation in Pgp overexpressing cells warrants further investigation of this class of compounds as clinical **modulators** of MDR.

L7 ANSWER 107 OF 141 CANCERLIT

L7 ANSWER 103 OF 141 MEDLINE DUPLICATE 60
ACCESSION NUMBER: 97029038 MEDLINE
DOCUMENT NUMBER: 97029038 PubMed ID: 8875050
TITLE: DiOC2(3) is not a substrate for **multidrug resistance** protein (**MRP**)-mediated drug efflux.
AUTHOR: Minderman H; Vanhoefer U; Toth K; Yin M B; Minderman M D; Wrzosek C; Slovak M L; Rustum Y M
CORPORATE SOURCE: Department of Experimental Therapeutics, Grace Cancer Drug Center, Roswell Park Cancer Institute, Buffalo, New York 14263, USA.
SOURCE: CYTOMETRY, **(1996 Sep 1)** 25 (1) 14-20.
Journal code: D92; 8102328. ISSN: 0196-4763.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19990129
Entered Medline: 19970218

AB Multidrug resistance (MDR) is often related to expression of P-glycoprotein (Pgp) or Multidrug Resistance Protein (MRP). Pgp-mediated MDR can be evaluated by determining cellular retention of fluorescent substrates by flow cytometry. This study determined if agents used to evaluate Pgp function also can be used to evaluate MRP function. Cellular retention of doxorubicin (Dox), Rhodamine-123 (Rh-123), and 3,3'-diethyloxacarbocyanine iodide (DiOC2(3)) were studied in MRP-expressing cell lines (HL60/Adr and HT1080/DR4), whereas a Pgp expressing cell line (A2780/Dx5) served as a positive control. Overexpression of Pgp correlated inversely with retention of Dox, Rh-123, and DiOC2(3); however, under identical experimental conditions (1 h reincubation in drug-free medium), no retention difference of the three agents was detected between parental and MRP-expressing resistant cells. Upon extending the reincubation time to 4 h, an efflux of Rh-123 and Dox in the resistant lines became apparent and even more pronounced after 24h; however, still no efflux was detectable for DiOC2(3). Incubation of the cells with a **modulator** of MDR, PAK-104P, negated the observed drug efflux in Pgp and MRP expressing cells, which correlated with increased sensitivity of the MDR lines to doxorubicin. Thus both Dox and Rh-123 can be used to evaluate MRP-function, but DiOC2(3) can not.

L7 ANSWER 104 OF 141 MEDLINE DUPLICATE 61

L7 ANSWER 99 OF 141 MEDLINE DUPLICATE 57
ACCESSION NUMBER: 96184396 MEDLINE
DOCUMENT NUMBER: 96184396 PubMed ID: 8612802
TITLE: Transport properties of the **multidrug resistance**-associated protein (**MRP**) in human tumour cells.
AUTHOR: Hollo Z; Homolya L; Hegedus T; Sarkadi B
CORPORATE SOURCE: National Institute of Haematology and Immunology, Budapest, Hungary.
SOURCE: FEBS LETTERS, **(1996 Mar 25)** 383 (1-2) 99-104.
Journal code: EUH; 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960613
Last Updated on STN: 19970203
Entered Medline: 19960606

AB In this paper we demonstrate that the expression of the multidrug resistance-associated protein (MRP) in a variety of intact human tumour cells results in the ATP-dependent, mutually exclusive extrusion of both the acetoxymethyl ester and the free anion forms of the fluorescent dye calcein, as well as that of a fluorescent pyrenemaleimide-glutathione conjugate. The MRP-dependent transport of all these three model compounds closely correlates with the expression level of MRP and is cross-inhibited by hydrophobic anticancer drugs, by **reversing** agents for MDR1, and also by compounds not influencing MDR1, such as hydrophobic anions, alkylating agents, and inhibitors of organic anion transporters. Cellular glutathione depletion affects neither the MRP-dependent extrusion of calcein AM or free calcein, nor its **modulation** by most hydrophobic or anionic compounds, although eliminating the cross-inhibitory effect of glutathione conjugates. These results suggest that the outward pumping of both hydrophobic uncharged and water-soluble anionic compounds, including glutathione conjugates, is an inherent property of MRP, and offer sensitive methods for the functional diagnostics of this transport protein as well as for the rapid screening of drug-resistance **modulating** agents.

L7 ANSWER 98 OF 141 MEDLINE DUPLICATE 56
ACCESSION NUMBER: 96326622 MEDLINE
DOCUMENT NUMBER: 96326622 PubMed ID: 8706899
TITLE: Transport of the glutathione conjugate of ethacrynic acid by the human **multidrug resistance** protein **MRP**.
AUTHOR: Zaman G J; Cnubben N H; van Bladeren P J; Evers R; Borst P
CORPORATE SOURCE: Division of Molecular Biology, Netherlands Cancer Institute, Amsterdam, The Netherlands.
SOURCE: FEBS LETTERS, **(1996 Aug 5)** 391 (1-2) 126-30.
Journal code: EUH; 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 19970203
Entered Medline: 19960912

AB The multidrug resistance protein MRP has been shown to mediate the transport of glutathione S-conjugates across membranes. In this study we demonstrate that the glutathione S-conjugate of the diuretic drug ethacrynic acid, which is an efficient inhibitor of glutathione S-transferases, is a high-affinity substrate and inhibitor of the glutathione S-conjugate pump associated with MRP. This implies that ethacrynic acid may **modulate** drug resistance of tumor cells not only by inhibiting glutathione S-transferase activity, but also by inhibiting the export of drug conjugates from the cell by MRP.

L7 ANSWER 99 OF 141 MEDLINE DUPLICA

L7 ANSWER 93 OF 141 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:256385 BIOSIS
DOCUMENT NUMBER: PREV199698812514
TITLE: VX-853: A novel bispecific chemosensitizer which **reverses** P-glycoprotein- and **MRP**-mediated **multidrug resistance**.
AUTHOR(S): Germann, U. A.; Shlyakhter, D.; Mason, V. S.; Ford, P. J.; Harding, M. W.
CORPORATE SOURCE: Vertex Pharmaceuticals Inc., Cambridge, MA 02139 USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (1996) Vol. 37, No. 0, pp. 335.
Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA
April
20-24, 1996
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L7 ANSWER 84 OF 141 MEDLINE DUPLICATE 49

ACCESSION NUMBER: 96296553 MEDLINE
DOCUMENT NUMBER: 96296553 PubMed ID: 8763341
TITLE: Experimental **modulation** of **MRP** (**multidrug resistance**-associated protein)-mediated resistance.
AUTHOR: Twentyman P R; Versantvoort C H
CORPORATE SOURCE: MRC Clinical Oncology and Radiotherapeutics Unit, Medical Research Council Centre, Cambridge, U.K.
SOURCE: EUROPEAN JOURNAL OF CANCER, **(1996 Jun)** 32A (6) 1002-9. Ref: 61
Journal code: ARV; 9005373. ISSN: 0959-8049.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961022
Last Updated on STN: 19961022
Entered Medline: 19961009

L7 ANSWER 79 OF 141 CANCERLIT
ACCESSION NUMBER: 96709614 CANCERLIT
DOCUMENT NUMBER: 96709614
TITLE: Reduced expression of the **multidrug resistance** protein, **MRP**, in human tumor cells by antisense oligonucleotides (Meeting abstract).
AUTHOR: Neverova I; Stewart A J; Canitrot Y; Baracchini E; Dean N M; Deeley R G; Cole S P
CORPORATE SOURCE: Cancer Res. Laboratories, Kingston, Ontario, K7L 3N6.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1996)**. Vol. 37, pp. A2113.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199610

AB Multidrug Resistance Protein (MRP) is overexpressed in many multidrug resistant cell lines and has been shown to cause multidrug resistance when transfected into previously sensitive cells. We have found that MRP mRNA and protein levels are reduced in transfected HeLa cells after treatment with MRP antisense oligonucleotides. Sixteen eicosomeric phosphorothioate oligonucleotides complementary to different regions along the entire length of the MRP mRNA were able to inhibit expression of MRP to some degree. One oligonucleotide, ISIS 7597 and two 'winged' 2' O-propyl derivatives ISIS 11471 and ISIS 9659, targeted to the coding region of the MRP mRNA, **decreased** MRP mRNA levels to less than 10% of control levels in a dose-dependent manner. This effect was transient and MRP mRNA levels returned to control levels less than 96 h after treatment. A double treatment with ISIS 7597 produced a sustained inhibition, resulting in a greater then 90% reduction in MRP mRNA for 72 h and a comparable **decrease** in protein levels. Increased sensitivity to doxorubicin was observed under these conditions. Northern blotting analyses using two DNA probes corresponding to sequence 5' and 3' of ISIS 7597 target sequence, respectively, revealed the presence of low levels of two smaller sized RNA fragments. These studies provide strong evidence for RNase H mediated destruction of a specific mRNA in intact cells following treatment with phosphorothioate oligonucleotides. They further suggest that antisense oligonucleotides may prove to be a feasible approach to circumvent resistance mediated by MRP.

L7 ANSWER 80 OF 141 MEDLINE DUPLICATE 46

L7 ANSWER 76 OF 141 CANCERLIT
ACCESSION NUMBER: 97608474 CANCERLIT
DOCUMENT NUMBER: 97608474
TITLE: VX-853: a novel bispecific chemosensitizer which **reverses** P-glycoprotein- and **MRP**-mediated **multidrug resistance** (Meeting abstract).
AUTHOR: Germann U A; Shlyakhter D; Mason V S; Ford P J; Harding M W
CORPORATE SOURCE: Vertex Pharmaceuticals Incorporated, Cambridge, MA 02139.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1996)**. Vol. 37, pp. A2283.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199704

AB Both the human multidrug resistance MDR1 gene product P-glycoprotein and the multidrug resistance-associated protein MRP have been associated with drug resistance in tumor cells and may represent major obstacles to successful cancer chemotherapy. VX-853 is a specifically designed MDR **reversing** agent that restores drug sensitivity in a variety of MDR1- or MRP-expressing multidrug resistant cells, including 8226/Dox6 myeloma cells, HL60/Vinc and HL60/ADR promyelocytic leukemia cells, MDR1 cDNA-transfected L1210vMDRC.06 leukemia cells and N3V2400 fibroblasts, and MRP cDNA-transfected 36-8-32 NIH 3T3 fibroblasts. In 3-day cytotoxicity or 14-day colony formation assays, VX-853 restores daunorubicin accumulation (IC50 0.2-0.4 uM) and blocks daunorubicin and rhodamine-123 efflux (IC50 0.3-0.6 uM) demonstrating the functional action of VX-853 on P-glycoprotein or MRP-mediated drug transport. Competitive displacement of P-glycoprotein-specific photoaffinity ligands by VX-853 and stimulation of P-glycoprotein ATPase activity by VX-853 (ka approx 50 nM) indicate a direct interaction of VX-853 with the MDR1 gene product. Inhibition of both MDR1- and MRP-mediated drug efflux by VX-853 suggests a greater potential for clinical benefit in treating patients with MDR cancers.

L7 ANSWER 75 OF 141 CANCERLIT
ACCESSION NUMBER: 96649891 CANCERLIT
DOCUMENT NUMBER: 96649891
TITLE: Differential activity of topoisomerase I inhibitors in **multidrug resistance** protein (**MRP**) and P170-glycoprotein (Pgp) mediated **multidrug resistance** (MDR) (Meeting abstract).
AUTHOR: Voigt W; Vanhoefer U; Yin M B; Hausheer F; Rustum Y M
CORPORATE SOURCE: Roswell Park Cancer Inst., Buffalo, NY 14263.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1996)**. Vol. 37, pp. A3013.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199608

AB The in vitro activity of topoisomerase I (Topo I) inhibitors camptothecin (CPT), SN-38, SN-22 and BNP1099 was evaluated in human ovarian carcinoma cell lines A2780 WT (parental) and 40-fold doxorubicin (Dox) resistant A2780 DX5 (Pgp+, MRP-) and fibrosarcoma cell lines HT1080 (parental) and 250 fold Dox resistant HT1080/DR4 (MRP+, Pgp-). Overexpression of Pgp and MRP was confirmed using Northern and Western blot analysis. The four Topo I inhibitors demonstrated no cross resistance in the MRP-mediated MDR cells. The A2780 DX5 cells were not cross resistant to SN-22 and BNP1099 and a 3-4 fold cross resistance against SN-38 and CPT could be completely **reversed** by the MDR-inhibitor PAK-200S. Topo I inhibiting activity was determined by drug inhibition assay where BNP1099 and SN-22 exerted the highest activity. A correlation between Topo I protein (Immunoblot) and specific activity of Topo I (DNA unwinding assay) was demonstrated for all cell lines. Topo I protein expression was lower in the A2780 DX5 as compared to the parental cell line but no significant difference was detected between HT1080 and HT1080/DR4 cells. Conclusions: (1) no cross resistance was seen with the Topo I inhibitors BNP1099 and SN-22 in MRP- and Pgp-mediated MDR, (2) CPT and SN-38 however exhibited low degree of cross resistance in Pgp-mediated MDR which could be completely **reversed** by PAK-200S, (3) Topo I protein expression and specific activity do not appear to correlate with the observed differences in drug activity.

L7 ANSWER 74 OF 141 CANCERLIT
ACCESSION NUMBER: 96649897 CANCERLIT
DOCUMENT NUMBER: 96649897
TITLE: CPT-11 sensitivity in relation to P170-glycoprotein (Pgp) and **multidrug-resistance** associated protein (**MRP**) expression investigated in vitro and in human tumor xenografts (Meeting abstract).
AUTHOR: Jansen W J; Hulscher T M; Giaccone G; Pinedo H M; Boven E
CORPORATE SOURCE: Dept. of Medical Oncology, Academic Hosp. Vrije Universiteit, Amsterdam, The Netherlands.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1996)**. Vol. 37, pp. A3019.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199608
AB CPT-11 has been reported to have a low level of cross-resistance in Pgp-positive cell lines in vitro, but not in Pgp-positive tumors in vivo. We studied the relevance of Pgp as well as MRP for the sensitivity to CPT-11 in the Pgp-positive BRO/mdr1.1 and 2780AD cell lines and the MRP-positive SW1573/S1 (MRP) and GLC4/ADR cell lines. The antiproliferative effects of CPT-11 +/- carboxylesterase (CE, 1 ug/ml) were measured by means of the MTT assay. The Pgp-positive cells showed a 25-fold resistance to CPT-11 + CE when compared to the sensitive cells. Addition of Pgp-**modulators** at non-toxic concentrations could **reverse** this resistance. From the results in the SW1573/S1 (MRP) and GLC4/ADR cells it appeared that CPT-11 +/- CE was not a substrate of MRP. Parent and Pgp-positive cells were grown as bilateral sc xenografts in nude mice. CPT-11 20 mg/kg ip daily x 5 was started when tumors measured approx 150 mm3. Efficacy was expressed as % growth inhibition (100%-treated/control%). BRO/mdr1.1 tumors were similarly sensitive to CPT-11 than BRO tumors. However, 2780AD tumors were less sensitive than A2780 tumors. This could be attributed to a 2.5-fold lower topoisomerase I activity in 2780AD cells. In conclusion, (1) Pgp expression is related to a low degree of cross-resistance to CPT-11 in vitro, but not in vivo; (2) MRP expression does not appear to affect the sensitivity to CPT-11.

L7 ANSWER 75 OF 141 CANCERLIT

L7 ANSWER 72 OF 141 MEDLINE DUPLICATE 45
ACCESSION NUMBER: 97332562 MEDLINE
DOCUMENT NUMBER: 97332562 PubMed ID: 9188796
TITLE: Anthracyclines **modulate multidrug resistance** protein (**MRP**) mediated organic anion transport.
AUTHOR: Heijn M; Hooijberg J H; Scheffer G L; Szabo G; Westerhoff H
V; Lankelma J
CORPORATE SOURCE: Academic Hospital Vrije Universiteit, Department of Medical
Oncology, Amsterdam, The Netherlands.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, **(1997 May 22)** 1326 (1) 12-22.
Journal code: A0W; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970716
Last Updated on STN: 19970716
Entered Medline: 19970702

AB We studied the ATP-dependent uptake of dinitrophenyl-glutathione (GS-DNP) into plasma membrane vesicles derived from parental GLC4 cells and from multidrug resistant GLC4/ADR cells. The latter have a high expression of the multidrug resistance protein (MRP). Uptake of GS-DNP into membrane vesicles from GLC4/ADR cells was highly stimulated by the addition of ATP, compared to the uptake into membrane vesicles from GLC4 cells. This ATP-dependent uptake into membrane vesicles from GLC4/ADR cells was saturable with a Km of 1.2 +/- 0.2 microM and a Vmax of 560 +/- 80 pmol/mg prot./min. ATP stimulated GS-DNP uptake with a Km of 187 +/- 4 microM. This uptake was specifically inhibited by a polyclonal serum raised against a fusion protein containing a segment of MRP. The ATP-dependent uptake of GS-DNP was not only inhibited by organic anions, such as oxidized glutathione (GSSG), methotrexate (MTX) and some bile acids, but also by non-anionic natural product drugs, such as anthracyclines, vinca alkaloids and etoposide (VP-16). Uptake of GSSG and MTX into membrane vesicles from GLC4/ADR cells could be stimulated by ATP. The ATP-dependent uptake of GSSG had a Km of 43 +/- 3 microM and a Vmax of 900 +/- 200 nmol/mg protein/min. The ATP-dependent uptake of GS-DNP seemed to be non-competitively inhibited by the anthracycline daunorubicin (DNR), whereas the ATP-dependent GSSG uptake seemed to be competitively inhibited by DNR. A substrate binding site on MRP is proposed that comprises a pocket in which both DNR and GS-DNP or GSSG bind in random order to different, only partly overlapping sites. In this pocket binding of a second compound is influenced by the compound which was bound first.

L7 ANSWER 73 OF 141 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

L7 ANSWER 70 OF 141 MEDLINE DUPLICATE 43
ACCESSION NUMBER: 1998070912 MEDLINE
DOCUMENT NUMBER: 98070912 PubMed ID: 9405241
TITLE: The quinoline-based drug, N-[4-[1-hydroxy-2-(dibutylamino)ethyl] quinolin-8-yl]-4-azidosalicylamide, photoaffinity labels the **multidrug resistance** protein (**MRP**) at a biologically relevant site.
AUTHOR: Vezmar M; Deady L W; Tilley L; Georges E
CORPORATE SOURCE: Institute of Parasitology, McGill University, Macdonald Campus, Ste-Anne de Bellevue, Quebec, Canada.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, **(1997 Dec 8)** 241 (1) 104-11.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980129
Last Updated on STN: 19980129
Entered Medline: 19980115

AB MRP is a member of the ABC trafficking proteins thought to mediate the transport of glutathione S-conjugates and amphiphilic natural products. However, unlike P-glycoprotein, the biochemical mechanism by which MRP mediates the resistance to cytotoxic drugs is not clear. In this report, we describe the interactions of a quinoline-based drug, N-4-[1-hydroxy-2-(dibutylamino)ethyl] quinolin-8-yl -4-azidosalicylamide (IAAQ), with MRP. Our results demonstrate the ability of IAAQ to photoaffinity label a 190 kDa protein in resistant Small Cell Lung Cancer cells (H69/AR) but not in the parental H69 cells. The photoaffinity labeling of the 190 kDa protein with IAAQ was both saturable and specific.

The identity of the 190 kDa protein, as MRP, was confirmed by immunoprecipitation with the monoclonal antibody, QCRL-1. Furthermore, a molar excess of LTC4, MK 571 or vinblastine inhibited the photoaffinity labeling of MRP with IAAQ in intact cells and plasma membranes. Cell growth and drug transport studies showed H69/AR cells to be less sensitive to and to accumulate less IAAQ than the parental H69 cells. In addition, MK 571 and doxorubicin increased the sensitivity to and the accumulation of IAAQ in H69/AR cells. Together, the results of this study show for the first time the direct binding of unaltered cytotoxic drug to MRP. Moreover, given the structural similarities between IAAQ and MK 571, we suggest that MK 571 **modulates** MRP-mediated resistance by direct binding to MRP.

L7 ANSWER 67 OF 141 MEDLINE DUPLICATE 40
ACCESSION NUMBER: 97226040 MEDLINE
DOCUMENT NUMBER: 97226040 PubMed ID: 9073310
TITLE: Chemosensitization and drug accumulation effects of VX-710,
verapamil, cyclosporin A, MS-209 and GF120918 in **multidrug resistant** HL60/ADR cells expressing the **multidrug resistance**-associated protein **MRP**.
AUTHOR: Germann U A; Ford P J; Shlyakhter D; Mason V S; Harding M W
CORPORATE SOURCE: Vertex Pharmaceuticals Inc., Cambridge, MA 02139-4242, USA.
SOURCE: ANTI-CANCER DRUGS, **(1997 Feb)** 8 (2) 141-55.
Journal code: A9F; 9100823. ISSN: 0959-4973.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970616

AB Overexpression of the multidrug resistance MDR1 gene product P-glycoprotein and/or the multidrug resistance-associated protein MRP confers multidrug resistance to cancer cells. The pipecolinate derivative VX-710 has previously been demonstrated to **reverse** MDR1-mediated multidrug resistance at concentrations of 0.5-2.5 microM by direct interaction with P-glycoprotein and inhibition of its drug efflux activity. In this study we investigated whether VX-710 as well as four other known MDR1 **modulators** could also **reverse** multidrug resistance mediated by MRP. VX-710 at 0.5-5 microM restored senstivity of MRP-expressing HL60/ADR promyelocytic leukemia cells to the cytotoxic action of doxorubicin, etoposide and vincristine. VX-710 was approximately 2-fold more effective than verapamil, MS-209 and CsA in **modulating** MRP-mediated multidrug resistance, whereas GF120918 had no significant effect. VX-710 was also more effective than verapamil, MS-209 and CsA in restoring the daunorubicin accumulation deficit in HL60/ADR cells and in increasing calcein uptake. A photoaffinity analog of VX-710, [3H]VF-13,159, specifically photo labeled the MRP protein and unlabeled VX-710 inhibited this binding in a concentration-dependent manner. These data suggest that VX-710 is not only a potent **modulator** of P-glycoprotein-mediated multidrug resistance, but also affects multidrug resistance in MRP-expressing cells and may exert its action, at least in part, by binding directly to MRP.

L7 ANSWER 62 OF 141 MEDLINE DUPLICATE 36
ACCESSION NUMBER: 97418083 MEDLINE
DOCUMENT NUMBER: 97418083 PubMed ID: 9272120
TITLE: A novel quinoline derivative, MS-209, overcomes **drug resistance** of human lung cancer cells expressing the **multidrug resistance** -associated protein (**MRP**) gene.
AUTHOR: Narasaki F; Oka M; Fukuda M; Nakano R; Ikeda K; Takatani H;
Terashi K; Soda H; Yano O; Nakamura T; Doyle L A; Tsuruo T;
Kohno S
CORPORATE SOURCE: Second Department of Internal Medicine, Nagasaki University
School of Medicine, Japan.
SOURCE: CANCER CHEMOTHERAPY AND PHARMACOLOGY, **(1997)** 40 (5) 425-32.
Journal code: C9S; 7806519. ISSN: 0344-5704.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 19970922
Entered Medline: 19970910

AB PURPOSE AND METHODS: MS-209 is a newly synthesized quinoline compound used orally to overcome human P-glycoprotein (Pgp)-mediated multidrug resistance (MDR). The multidrug resistance-associated protein (MRP) gene is thought to play an important role in MDR in lung cancer. To investigate whether MS-209 could also overcome MRP-mediated MDR, we examined the effect of the compound using a cytotoxicity assay on MDR1 gene-negative drug-selected MDR and wildtype lung cancer cells with various levels of MRP gene expression. The effects of MS-209 were compared with those of verapamil (VER) and cyclosporin A (CsA). The level of MRP gene expression in the cells was evaluated semiquantitatively by RT-PCR. For vincristine (VCR), intracellular accumulation of [3H]-VCR was measured with or without MS-209. RESULTS: In MDR UMCC-1/VP small-cell lung carcinoma cell line, 5 microM of MS-209 and VER enhanced the cytotoxicity of etoposide, doxorubicin (DOX) and VCR more than twofold, and completely **reversed** the resistance to VCR. The mean **reversing** effects of MS-209 on DOX and VCR were significantly stronger than those of VER and CsA. In wildtype non-small-cell lung carcinoma cells, the effects of MS-209 were almost equal to those of VER and CsA. The effect of these three agents correlated with the level of MRP gene expression. The MS-209-induced increase in intracellular accumulation of VCR was proportional to the level of MRP gene expression in these cells. CONCLUSION: Our results indicate that MS-209 is a potentially useful drug that can overcome MRP-mediated intrinsic and acquired MDR in human lung cancer.

L7 ANSWER 63 OF 141 CANCERLIT

L7 ANSWER 39 OF 141 CANCERLIT
ACCESSION NUMBER: 1998640215 CANCERLIT
DOCUMENT NUMBER: 98640215
TITLE: Diverse effects of tumor necrosis factor alpha on expression of the **multidrug resistance** -associated genes LRP and **MRP** (Meeting abstract).
AUTHOR: Stein U; Walther W; Laurencot C M; Scheffer G L; Scheper R J; Shoemaker R H
CORPORATE SOURCE: Max-Delbrueck-Center for Molecular Medicine, Berlin, Germany 13122.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A3215.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199803

AB lt has previously been shown that treatment of multidrug resistant human tumor cells with cytokines can result in their sensitization towards drugs. Recently, we have reported that in vitro treatment of colon carcinoma cells with human tumor necrosis factor alpha (TNF) or transduction of the human TNF gene is associated with reduced expression of the mdr1 gene at the mRNA, protein and functional level. To investigate this phenomenon in relation to the more recently described MDR-associated genes LRP (lung resistance protein) and MRP (multidrug resistance associated protein), we evaluated the effect of TNF on the mRNA level by RT-PCR and on the protein level by immuno flow cytometry. Human colon carcinoma cell lines HCT15 and HCT116 were incubated with TNF for 2, 12, 24, 48 or 72 hours, or were transduced with the human TNF gene. **Modulated** expression of LRP and MRP was observed under both treatment conditions: LRP expression was reduced by TNF in an apparently time- and dose-related fashion. In contrast, MRP expression was increased on both expression levels. These results illustrate the complexity of multiple MDR phenotypes, which may coexist within a tumor cell population. They further suggest that strategies for **reversal** of MDR should not focus exclusively on the mdr1 gene, but should also address the net effect of MDR mechanisms which may respond in coordinate, or contrasting ways to **modulating** agents.

L7 ANSWER 38 OF 141 CANCERLIT
ACCESSION NUMBER: 1998640968 CANCERLIT
DOCUMENT NUMBER: 98640968
TITLE: The steroidal agent ZK112993 inhibits the **multidrug resistance** (MDR) phenotype associated with the expression of the **multidrug resistance** protein (**MRP**) (Meeting abstract).
AUTHOR: Leonessa F; Green G; Lippman J; Clarke R
CORPORATE SOURCE: Vincent T Lombardi Cancer Center, Georgetown University Medical Center, Washington, DC 20007.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A3968.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199802
AB 17beta-estradiol-17(beta-D-glucuronide) (E2G) is implicated as a substrate for MRP. Thus, steroids, by a competitive mechanism, may interfere with the MDR phenotype conferred by MRP. We tested the chemosensitizing activity of several steroids on MCF7/VP, a cell line derived by selection of MCF-7 human breast cancer cells with etoposide. MCF7/VP cells exhibit an MDR phenotype, and express MRP, but not P-glycoprotein. Estrone, estrone-3-sulfate, 17beta-estradiol, E2G, progesterone, hydrocortisone, cholesterol and 5-choleric acid-3beta-ol, at achievable non-toxic concentrations, did not show any significant chemosensitizing activity with respect to doxorubicin (Dx). However, we observed a 1.7 fold sensitization by ZK112993, a steroidal antiprogestational agent carrying a bulky moiety including an aromatic ring at the C11 position. Further evaluations confirmed that ZK112993 increases the cytotoxic effect of Dx in MCF7/VP and, to a much lesser extent, in MCF-7 cells. Even after correction for the a specific effect, results show that ZK112993 causes a dose-dependent sensitization in MCF7/VP cells, which reaches more than 2-fold at 5 uM. Isobologram analysis confirmed that interaction is synergistic, as would be predicted for a MRP-**reversing** agent, and that the increased inhibition is not the result of additive toxicity.

L7 ANSWER 36 OF 141 CANCERLIT
ACCESSION NUMBER: 1998640974 CANCERLIT
DOCUMENT NUMBER: 98640974
TITLE: Synergistic effects of doxorubicin and **modulators** of **multidrug resistance** in small cell lung cancer (SCLC) cells naturally expressing MDR-1, **MRP** and LRP phenotypes (Meeting abstract).
AUTHOR: Chan D; Helfrich B; Helm K; Chou T; Bunn P
CORPORATE SOURCE: Univ. of Colorado Cancer Center, Denver, CO 80262.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A3974.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199802

AB In this report we have evaluated six different MDR **modulators** including Verapamil (Vpm), Dexverapamil (Dvpm), Cyclosporin A (CSA), PSC 833 (P833), Niguldipine (Ngd) and Dexniguldipine (Dngd) in a SCLC cell line SHP 77 which has a classical MDR phenotype. It has a reduced Rhodamine R123 uptake and a reduced sensitivity to doxorubicin when compared to other SCLC cell lines that do not have MDR. This cell line was established from a patient before chemotherapy. It has not been exposed to drug selection and has elevated expression of MDR (50%+), LRP (49%+) and MRP (29%) phenotype, as demonstrated with three different monoclonal antibodies (Mab 4E3, MRPm6 and LRP-56). Cells were treated with doxorubicin from 0.001 to 2 ug/ml in the absence or presence of the **modulator** ranging from 0.001 to 20 uM. MTT growth assay was used to measure the cytotoxicity of the agents. The data were then analyzed by a CalcuSyn software using the combination index-isobologram method, which is based on the median-effect principle (TIP Sci 4:450 1983). Mutually exclusive (conventional) isobologram was used to calculate the combination-indexes (CI), where CI more than 1, CI=1 CI less than 1 indicates **antagonism**, additive effect and synergism. Strong synergisms were found for all of these agents with potencies ranking as CSA more than Vpm more than Dngd more than Dvpm more than P833 more than Ngd. However, because of the unfavorable side-effects from CSA (immunosuppressive), Vpm and Ngd (cardiovascular toxicities), we conclude that the other three agents Dngd more than Dvpm more than P833 may provide a better clinically achievable **modulatory** effects for chemosensitizer treatment of cancer patients.

L7 ANSWER 35 OF 141 CANCERLIT
ACCESSION NUMBER: 1998640989 CANCERLIT
DOCUMENT NUMBER: 98640989
TITLE: **Reversal** of **MRP**-associated **drug resistance** by the pyridine analog, PAK-104P (Meeting abstract).
AUTHOR: Chuman Y; Chen Z S; Sumizawa T; Seto K; Furukawa T; Haraguchi M; Tani A; Shudo N; Yamada K; Akiyama S; Aikou T
CORPORATE SOURCE: Kagoshima University, Sakuragaoka 8-35-1, Kagoshima 890, Japan.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, **(1997)**. Vol. 38, pp. A3989.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199802

AB Three agents, verapamil, cepharanthine and 2-[4-(diphenylmethyl)-1-piperazinyl]ethyl 5-(trans-4,6-dimethyl-1,3,2-dioxaphosphorinan-2-yl)-2,6-di methyl-4-(3-nitrophenyl)-3-pyridinecarboxylate P-oxide (PAK-104P), that **reverse** drug resistance in P-glycoprotein (P-gp)-mediated multidrug resistant cells were examined for their activity to **reverse** drug resistance in multidrug resistance (MDR)-associated protein (MRP)-mediated multidrug resistant C-A120 cells. The agents other than PAK-104P could not **reverse** the resistance to doxorubicin (ADM) in C-A120 cells. PAK-104P moderately **reversed** the ADM resistance. In contrast, PAK-104P almost completely **reversed** the resistance to vincristine (VCR) in C-A120 cells as well as KB-8-5 cells and other agents moderately **reversed** the VCR resistance in C-A120 cells. PAK-104P at 10 uM enhanced the accumulation of VCR in C-A120 cells to the level of that in KB-3-1 cells without the agent. PAK-104P competitively inhibited the ATP-dependent [3H]leukotriene C4 uptake in membrane vesicles isolated from C-A120 cells. These findings demonstrate that PAK-104P can completely **reverse** the resistance to VCR in both P-gp- and MRP-mediated MDR cells, and that PAK-104P directly interacts with MRP and inhibits the transporting activity of MRP.

L7 ANSWER 30 OF 141 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 1998366080 MEDLINE
DOCUMENT NUMBER: 98366080 PubMed ID: 9700723
TITLE: Development of novel **reversal** agents, imidazothiazole derivatives, targeting MDR1- and **MRP**-mediated **multidrug resistance**.
AUTHOR: Naito S; Koike K; Ono M; Machida T; Tasaka S; Kiue A; Koga H; Kumazawa J
CORPORATE SOURCE: Department of Urology, Faculty of Medicine, Kyushu University, Fukuoka, Japan.. naito@uro.med.kyushu-u.ac.jp
SOURCE: ONCOLOGY RESEARCH, **(1998)** 10 (3) 123-32.
Journal code: BBN; 9208097. ISSN: 0965-0407.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981029

AB Three newly synthesized imidazothiazole derivatives (N276-12, N276-14, N276-17) were examined regarding their ability and mechanism as a chemosensitizing agent against multidrug resistance 1 (MDR1)-mediated and multidrug resistance-associated protein (MRP)-mediated MDR. All three N276 compounds almost completely **reversed** the acquired resistance to vincristine (VCR), vinblastine (VBL), and doxorubicin (DXR) in MDR1-overexpressing human cancer cell lines (KB/VJ300 and T24/VCR). Their **reversal** effect against acquired resistance to VCR, DXR, and etoposide (VP16) was partial but clearly observed in the cell line expressing MRP (KB/VP4). All three N276 compounds enhanced the intracellular accumulation of [3H]VCR in MDR1-overexpressing KB/VJ300 cells through the inhibition of the increased efflux of the drug. They (100 microM) almost completely inhibited the photoaffinity labeling of P-glycoprotein encoded by the MDR1 gene. All the N276 compounds also remarkably enhanced the sensitivity to VBL and DXR in both MDR1- and MRP-overexpressing renal cell carcinoma (RCC) cell line (NKK1), whereas they showed no potentiation of these anticancer agents in an RCC cell line (KPK1) expressing neither MDR1 nor MRP. The combination chemotherapy of VCR or VP16 with N276-12 significantly increased the life span of mice inoculated i.p. or i.v. with drug-resistant P388/VCR cells without any significant side effects, whereas chemotherapy with the anticancer agent alone did not increase the life span at all. These results suggest that these newly synthesized imidazothiazole derivatives can be a useful chemosensitizing agent against not only MDR1- but also MRP-mediated MDR.

L7 ANSWER 22 OF 141 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 1998379134 MEDLINE
DOCUMENT NUMBER: 98379134 PubMed ID: 9713512
TITLE: Co-transfection of MDR1 and **MRP** antisense RNAs abolishes the **drug resistance** in **multidrug-resistant** human lung cancer cells.
AUTHOR: Gao Z; Gao Z; Fields J Z; Boman B M
CORPORATE SOURCE: Cancer Research Laboratory, CA*TX, Inc., Omaha, NE 68103, USA.
CONTRACT NUMBER: R21 CA71531-02 (NCI)
SOURCE: ANTICANCER RESEARCH, **(1998 Jul-Aug)** 18 (4C) 3073-6.
Journal code: 59L; 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980910

AB The resistance of lung cancer cells to the therapeutic actions of anticancer drugs is a serious clinical problem often encountered during cancer chemotherapy. It is very important, therefore, to investigate how to prevent and/or **reverse** this drug resistance. To this end, we took advantage of the fact that the overexpression of MDR1 and MRP genes, two genes known to be associated with the development of drug resistance, is very common in lung cancer. We used antisense RNA in an attempt to prevent expression of the protein products of these genes. Using a retrovirus, we introduced the antisense RNAs of MDR1 and MRP genes into doxorubicin-selected, multidrug-resistant GAOK cells, a cell which overexpresses both MDR1 and MRP genes. The expression levels of the products of the MDR1 gene (Pgp) and MRP gene (Mrp) in the transfected cells were analyzed using flow cytometry, and the drug resistances of the transfected cells were detected by a cell viability (MTT) assay. The expression of Pgp and Mrp in the transfected cells was almost completely inhibited by the antisense RNAs: expression levels **decreased** 64% and 93%, respectively. In parallel, the drug resistance of these cells **decreased** about 99% to doxorubicin, 98% to vinblastine, and 97% to colchicine. These results show that: a) antisense RNAs can attenuate drug resistance, an inhibition that might lead to new treatments for patients who are, or become, refractory to conventional chemotherapy; b) MDR1 and MRP appear to be cooperating to confer drug resistance in GAOK cells.

L7 ANSWER 23 OF 141 MEDLINE DUPLICATE 17

L7 ANSWER 21 OF 141 CANCERLIT
ACCESSION NUMBER: 1998700915 CANCERLIT
DOCUMENT NUMBER: 98700915
TITLE: PROBENECID AS A POTENTIAL **MODULATOR** OF **DRUG RESISTANCE** IN THE **MRP** OVEREXPRESSING BREAST CANCER CELL LINE MCF7-VP (Meeting abstract).
AUTHOR: Dearden T; Chadderton A; Yan B; Bewick M; Rhude A; Parissenti A; Gluck S
CORPORATE SOURCE: The Northeastern Ontario Regional Cancer Centre, Sudbury, ON, Canada.
SOURCE: Proc Annu Meet Am Soc Clin Oncol, **(1998)**. Vol. 17, pp. A917.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199910

AB Numerous mechanisms of drug resistance in breast cancer have been described in the past. While the significance of these mechanisms in the clinical setting are unclear, means of **modulating** drug resistance in vitro are being explored. The Multidrug Resistance Associated Protein (MRP) has been shown to be capable of transporting a range of chemotherapeutic agents and has become a potential target of **reversing** agents. The breast cancer cell line MCF7-VP was selected by exposure to VP-16, and has been shown to overexpress MRP by 10 fold. In our study, MCF7-VP cells in liquid culture were exposed to media alone, Doxorubicin (DOX) (3uM), Probenecid (0.1mM) or a combination of DOX (3uM) and Probenecid (0.1mM, 0.01mM and 1uM). Cells were incubated for 24 hours after which an MTT cell viability assay was used. The following trends were found; DOX alone reduced mean cell viability by 15.6%, Probenecid resulted in a 5.3% loss in mean viable cells, while a 32.9% drop in mean cell viability was achieved when the 2 drugs were given in combination. In contrast, control experiments using the parental MCF7-WT and the Pgp-overexpressing MCF7-ADR cell lines showed in both cases that the addition of Probenecid had no effect on DOX drug sensitivity. Our results suggest the role of Probenecid as a potential **modulator** of drug resistance in breast cancer cells overexpressing MRP. These results are similar to those found in other, non-breast cancer MRP overexpressing cell lines and prompt further investigation. Additional experiments using a clonogenic assay are in progress. In conclusion, this work is the first to show that Probenecid, at clinically achievable and non-toxic concentrations, produces a **reversing** trend in the DOX resistance of the breast cancer cell line MCF7-VP. (C) American Society of Clinical Oncology 1998.

L4 ANSWER 3 OF 4 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 87033956 MEDLINE
DOCUMENT NUMBER: 87033956 PubMed ID: 3095338
TITLE: Relation between the regulation of DNA synthesis and the production of two secreted glycoproteins by 12-O-tetradecanoylphorbol-13-acetate in 3T3 cells and in phorbol ester nonresponsive 3T3 variants.
AUTHOR: Fienup V K; Jeng M H; Hamilton R T; Nilsen-Hamilton M
CONTRACT NUMBER: CA39256 (NCI)
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, **(1986 Nov)** 129 (2) 151-8.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198612
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 20020420
Entered Medline: 19861215

AB 12-O-tetradecanoylphorbol-13-acetate (TPA), a potent tumor promoter, acts similarly to growth factors by selectively increasing the rate of production of the secreted proteins, mitogen regulated protein (MRP) and major excreted protein (MEP) by murine 3T3 cells. MRP, a 34 kilodalton (kDa) glycoprotein, is a member of the prolactin-growth hormone family of proteins. MEP, a 39 kDa glycoprotein, is a lysosomal thiol protease that is also secreted. The aim of our investigation was to determine the relation between increases in MRP and MEP production and the initiation of DNA synthesis in response to mitogens. The TNR-9 cell line is a variant of 3T3 cells in which growth factors, but not TPA and teleocidin, stimulate DNA synthesis and cell division. Using [35S]methionine to metabolically label proteins and SDS polyacrylamide gel electrophoresis to resolve the proteins, we found that growing cultures of 3T3 and TNR-9 cells responded equally well to TPA and teleocidin with increased rates of production of MRP and MEP. By contrast, the responses of quiescent TNR-9 cells to these tumor promoters in the increased production of MRP and MEP was greatly diminished compared with quiescent 3T3 cells. The changes in production of MRP in response to tumor promoters in quiescent and growing cells paralleled similar changes in the level of MRP mRNA. In summary, the ability to TPA and teleocidin to increase the rate of production of MRP and MEP correlated with the ability of these tumor promoters to stimulate DNA synthesis in quiescent 3T3 and TNR-9 cells. Evidently the biochemical condition that distinguishes TNR-9 from 3T3 cells and that limits the ability of tumor promoters to stimulate the production of MEP and MRP, and perhaps also DNA synthesis in TNR-9 cells occurs only when the cells are quiescent.

L17 ANSWER 13 OF 15 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 92251199 MEDLINE
DOCUMENT NUMBER: 92251199 PubMed ID: 1374453
TITLE: Cloning of a novel tumor necrosis factor-alpha-inducible primary response gene that is differentially expressed in development and capillary tube-like formation in vitro.
AUTHOR: Sarma V; Wolf F W; Marks R M; Shows T B; Dixit V M
CORPORATE SOURCE: Department of Pathology, University of Michigan Medical School, Ann Arbor 48109.
CONTRACT NUMBER: HL45351 (NHLBI)
SOURCE: JOURNAL OF IMMUNOLOGY, **(1992 May 15)** 148 (10) 3302-12.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-M92357
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920619
Last Updated on STN: 19960129
Entered Medline: 19920609

AB TNF is a proinflammatory cytokine that has pleiotropic effects on cells and tissues, mediated in large part by alterations in target tissue gene expression. We have used the technique of differential hybridization to identify several primary response genes induced by TNF in human umbilical vein endothelial (HUVE) cells, a cell type that is profoundly activated by cytokine treatment. One of these cDNA, designated **B94**, detects a rapidly and transiently induced 4-kb transcript in TNF-treated HUVE cells, and this transcript is superinduced in the concomitant presence of cycloheximide. Other proinflammatory stimuli including IL-1 beta and LPS are also able to induce **B94** mRNA expression. Nuclear run-on experiments demonstrate that TNF induction of **B94** transcript occurs primarily at the level of transcriptional activation. Further, **B94** is shown to be a single copy gene that is evolutionarily conserved. The gene is localized to the q32 region of chromosome 14, a region that is often rearranged in lymphoid neoplasms. **B94** transcript expression is also found to be regulated during mouse development and in an in vitro model of endothelial capillary tube formation. Developmental regulation occurs most prominently in mouse embryonic liver and kidney, and a second smaller form of **B94** transcript is detected in the placenta and testes. **B94** and other TNF-responsive transcripts are also induced during capillary tube formation suggesting overlap between genes induced by TNF and those induced during angiogenesis. Sequence analysis of the **B94** cDNA reveals an open reading frame encoding a 73-kDa polypeptide that has no homology to any known protein. Polyclonal antisera directed against the carboxyl-terminal portion of the **B94** protein immunoprecipitates a protein of the predicted molecular mass both from COS cells transfected with a **B94** expression vector and from TNF-treated HUVE cells.

L17 ANSWER 8 OF 15 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 94148868 MEDLINE
DOCUMENT NUMBER: 94148868 PubMed ID: 8106408
TITLE: **B94**, a primary response gene inducible by tumor necrosis factor-alpha, is expressed in developing hematopoietic tissues and the sperm acrosome.
AUTHOR: Wolf F W; Sarma V; Seldin M; Drake S; Suchard S J; Shao H; O'Shea K S; Dixit V M
CORPORATE SOURCE: Department of Pathology, University of Michigan Medical School, Ann Arbor 48109.
CONTRACT NUMBER: HL45351 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1994 Feb 4)** 269 (5) 3633-40.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L24118
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940330
Last Updated on STN: 19940330
Entered Medline: 19940318

AB **B94** was originally described as a novel tumor necrosis factor-alpha-inducible primary response gene in endothelial cells which was also induced in an in vitro model of angiogenesis. To further characterize its expression, we cloned the mouse homologue and mapped its developmental and tissue specific expression. The predicted amino acid sequence of mouse **B94** was found to be 83% similar to its human homologue. The gene was localized to mouse chromosome 12 just centromeric to the immunoglobulin heavy chain locus, in a region that is often rearranged in T-cell neoplasms. To explore the possibility that **B94** is expressed during vasculogenesis and other developmental processes, the expression of its transcript was determined during mouse development by in situ hybridization. In 10-day embryos **B94** was expressed prominently in the myocardium and in the aortic arch. By the 15th day of gestation, expression was restricted largely to the liver, the bone forming regions of the jaw, the aortic endothelium, and the nasopharynx: a pattern that was maintained until just prior to birth. Postnatally, expression shifted to the red pulp of the spleen and the thymic medulla. **B94** expression was extinguished in most adult tissues but was detectable in lymphopoietic tissues including the spleen, tonsil, and lymphatic aggregates in the gut. Consistent with this was the finding that mononuclear progenitor cells in bone marrow and mature peripheral blood monocytes expressed **B94**. A truncated testis-specific transcript previously identified by Northern blot analysis was determined to result from the use of an alternate polyadenylation signal which was surprisingly located within the open reading frame. This shorter transcript was expressed at high levels exclusively in late stage spermatids. Immunostaining with an affinity-purified polyclonal antiserum revealed **B94** to be localized to the acrosomal compartment of mature sperm. These studies demonstrate that **B94** expression is tightly regulated during development and suggests distinct roles for **B94** in myelopoiesis and spermatogenesis.

L24 ANSWER 17 OF 18 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 92028985 MEDLINE
DOCUMENT NUMBER: 92028985 PubMed ID: 1834059
TITLE: Mouse oncogene protein **24p3** is a member of the lipocalin protein family.
AUTHOR: Flower D R; North A C; Attwood T K
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Leeds, UK.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1991 Oct 15) 180 (1) 69-74.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199111
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911121

AB Rigorous new methods of protein sequence analysis have been applied to the lipocalins, a diverse family of ligand binding proteins. Using three conserved sequence motifs to search for similar patterns in a large sequence database, the size and composition of this protein family have been defined in an automatic and objective way. It has allowed the identification of an existing sequence, mouse 24p3 protein, as a lipocalin and the possible rejection of other putative members from this protein family. On the basis of this newly discovered homology, a possible function for mouse 24p3 protein is proposed.

L24 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:232177 BIOSIS
DOCUMENT NUMBER: PREV199799531380
TITLE: High expression of the lipocalin **24p3** correlates with negative ER and PgR levels in breast cancer cells in vivo and in vitro.
AUTHOR(S): Chen, K.-S. (1); Stoesz, S. P.; Lindstrom, M. J.; Clark, G.
M.; Gould, M. N.
CORPORATE SOURCE: (1) Dep. Human Oncol., Madison, WI 53792 USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (1997) Vol. 38, No. 0, pp. 294.
Meeting Info.: Eighty-eighth Annual Meeting of the American
Association for Cancer Research San Diego, California, USA April 12-16, 1997
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L24 ANSWER 8 OF 18 CANCERLIT
ACCESSION NUMBER: 1998638976 CANCERLIT
DOCUMENT NUMBER: 98638976
TITLE: High expression of the lipocalin **24p3** correlates with negative ER and PgR levels in breast cancer cells in vivo and in vitro (Meeting abstract).
AUTHOR: Chen K-S; Stoesz S P; Lindstrom M J; Clark G M; Gould M N
CORPORATE SOURCE: Univ. Winsconsin-Madison, Depts. of Human Oncology and Biostatistics, Madison, WI 53792.
SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1997). Vol. 38, pp. A1976.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199803

AB The lipocalin 24p3 has been previously reported to be associated with highly aggressive neu-induced rat mammary carcinomas. In order to extend this investigation to human breast cancer, we characterized 120 human breast carcinomas for HER2/neu amplification and 24p3 expression. Surprisingly, we found no correlation (p=0.5624). However, we did find a strong association between high 24p3 levels and ER- (p=0.0001) and PgR-negative status (p=0.0004) and high S-phase fraction (p=0.0011) in 250 breast cancer patients. These observations were extended to several breast cancer cell lines. Cell lines negative for ER and PgR, MDA:MB-231 and T47D:C4:2W, had high levels of 24p3, while cell lines positive for both steroid receptors, T47D:A18 and MCF-7:WS8, expressed little or no 24p3. We are currently characterizing the human and rat 5' region of the 24p3 gene to delineate mechanisms underlying these observations. Both 5' regions have been cloned and sequenced, and found to contain several consensus binding sequences for transcriptional factors, including TATA-like box, NF-1 and NF-kB binding sites, and two negative GRE/PRE elements. These results suggest that 24p3 has the potential to serve as a downstream marker of ER/PgR-negative status in breast cancer.

L24 ANSWER 9 OF 18 MEDLINE DUPLICATE 6

L10 ANSWER 60 OF 60 MEDLINE on STN DUPLICATE 34
ACCESSION NUMBER: 90321782 MEDLINE
DOCUMENT NUMBER: 90321782 PubMed ID: 2640156
TITLE: Correlation of inhibition of adhesion of large cell lymphoma and hepatic sinusoidal **endothelial** cells by **RGD**-containing **peptide** polymers with **metastatic** potential: role of integrin-dependent and -independent adhesion mechanisms.
AUTHOR: Tressler R J; Belloni P N; Nicolson G L
CORPORATE SOURCE: Department of Tumor Biology, University of Texas MD Anderson Cancer Center, Houston 77030.
CONTRACT NUMBER: P30-CA16672 (NCI)
R35-CA44352 (NCI)
SOURCE: CANCER COMMUNICATIONS, **(1989)** 1 (1) 55-63.
Journal code: 8916730. ISSN: 0955-3541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19901012
Last Updated on STN: 19970203
Entered Medline: 19900827

AB Murine RAW117 large-cell lymphoma cells that show organ preferences of **metastatic** colonization were selected. We examined the role of adhesive systems in determining the organ preference of **metastasis** using cell lines of low (RAW117-P) and high (RAW117-H10) liver-**metastatic** potential. Highly **metastatic** H10 cells adhered at higher rates than low **metastatic** P cells to target organ microvessel **endothelial** cells, and these interactions were partially inhibited by RGD-containing polymers but not by small peptides such as GRGDS or GRGES. The most effective polymers, such as (GRGDS)4 and GRGDS(GRGES)2GRGDS, significantly inhibited H10 cell adhesion but had less effect on P cell adhesion to target liver sinusoidal **endothelial** cell monolayers or on P cell or H10 cell adhesion to bovine aortic **endothelial** cell monolayers. The (GRGDS)4 polymer reduced the rate of H10 liver sinusoidal **endothelial** cell adhesion to that of P cells in the absence of inhibitors, suggesting that the quantitative difference in adhesion of H10 cells versus P cells to liver sinusoidal **endothelial** cells may have been due to integrin-like molecules. Other RGD-containing polymers, such as (GRGES)2(GRGDS)2, GRGES(GRGDS)2GRGES, or (GRGES)4, were less effective, suggesting that the secondary structure of the polymers may be an important consideration. A peptide from the B1 chain of laminin (YIGSR) or its homopolymer, (YIGSR)4, had no effect on **endothelial** cell adhesion, consistent with the lack of differential laminin adhesion seen with various RAW117 cell lines. The results suggest that integrin-related molecules may play a role in the organ specificity of **endothelial** cell adhesion seen with RAW117 **tumor** cells.

L10 ANSWER 59 OF 60 MEDLINE on STN DUPLICATE 33
ACCESSION NUMBER: 89234196 MEDLINE
DOCUMENT NUMBER: 89234196 PubMed ID: 2469686
TITLE: Human microvascular **endothelial** cells express integrin-related complexes that mediate adhesion to the extracellular matrix.
AUTHOR: Cheng Y F; Kramer R H
CORPORATE SOURCE: Department of Anatomy, School of Medicine, University of California, San Francisco 94143.
CONTRACT NUMBER: CA33834 (NCI)
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, **(1989 May)** 139 (2) 275-86.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890609

AB Microvascular **endothelial** cells (MEC) must use a set of surface receptors to adhere not only to the **vascular** basement membrane but, during **angiogenic** stimulation, to the interstitium. We examined how cultured MEC isolated from human foreskin interact with their subendothelial matrix. MEC were able to attach to diverse extracellular matrix proteins, including fibronectin (Fn), vitronectin (Vn), laminin (Ln), type I and IV collagen, as well as to fibrinogen and gelatin. Adhesion to Fn, but not to laminin or collagens, was specifically blocked in the presence of Arg-Gly-Asp (**RGD**)-containing **peptides**. When surface radioiodinated MEC were solubilized and subjected to affinity chromatography on Fn-Sepharose columns, two polypeptides of 150 and 125 kD, corresponding to the integrin heterodimer alpha 5 beta 1, were identified. MEC also express a complex of 150 (alpha) and 95 kD (beta 3) that is related to the Vn receptor. Immunofluorescent staining of MEC cultures with antibodies to the integrin beta 1 subunit demonstrated receptors on the basolateral surface at focal adhesion plaques that co-localized with vinculin and with Fn-positive matrix fibers. Occasionally, antibodies to the Vn receptor stained the vinculin-positive focal adhesion plaques that frequently co-localized with the beta 1 complex. However, in cultures of MEC that were attached to substrates coated with alternating strips of Fn and Vn, the beta 1 complex was preferentially localized to the Fn substrate, while the Vn receptor was concentrated on the Vn substrate. The results indicate that MEC express at least two different heterodimer adhesion receptors that belong to the integrin super-family and appear to have distinct ligand specificities: the Fn receptor and the Vn receptor. These receptors mediate cell adhesion to the extracellular matrix and presumably have an important role in hemostasis and neovascularization.

L10 ANSWER 56 OF 60 MEDLINE on STN DUPLICATE 32
ACCESSION NUMBER: 91339170 MEDLINE
DOCUMENT NUMBER: 91339170 PubMed ID: 1908352
TITLE: Effect of inflammatory cytokines on the adherence of **tumor** cells to **endothelium** in a murine model.
AUTHOR: Bereta M; Bereta J; Cohen S; Zaifert K; Cohen M C
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Hahnemann University, Philadelphia, Pennsylvania 19102.
CONTRACT NUMBER: CA-32319 (NCI)
CA-39723 (NCI)
SOURCE: CELLULAR IMMUNOLOGY, **(1991 Sep)** 136 (2) 263-77.
Journal code: 1246405. ISSN: 0008-8749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19911013
Last Updated on STN: 19970203
Entered Medline: 19910920

AB We have demonstrated that pretreatment of mouse brain microvascular **endothelial** cells (MBE) with **tumor** necrosis factor-alpha (TNF), IL-1, or LPS augmented the binding of P815 mastocytoma cells in vitro. The effect of these agents was dose and time dependent. PMA was able to mimic the influence of these factors to a limited degree. The effect of TNF on **endothelium** was accompanied by the appearance of changes in the expression of proteins isolated from **endothelial** cell membranes. The adherence of **tumor** cells to **endothelium** was not inhibited by **RGD**-containing **peptides** but could be decreased by preincubation of **endothelium** with high concentrations of FCS. Our data suggest that cytokines regulate the synthesis of **endothelial** adhesion proteins which may be involved in **tumor** cell adherence leading to **metastasis**. These results raise the possibility that cytokines may exert paradoxical effects in vivo, i.e., a cytotoxic effect that reduces **tumor** mass accompanied by a **metastasis** -enhancing effect that actually promotes dissemination of the remaining **tumor** cells. Definition of the molecular events involved in **tumor** cell-**endothelial** cell interactions may lead to strategies for minimizing the latter effect in therapeutic settings.